“THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY AND ITS HISTOPATHOLOGICAL CORRELATION”

Dissertation submitted in

Partial fulfillment of the regulations required for the award of

M.D. DEGREE

In

PATHOLOGY – BRANCH III

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI.

APRIL 2017

DECLARATION

I hereby declare that the dissertation entitled **"THE BETHESDA SYSTEM OF REPORTING THYROID CYTOPATHOLOGY AND ITS HISTOPATHOLOGICAL CORRELATION**" is a bonafide research work done by me in the Department of Pathology, Coimbatore Medical College during the period from July 2015 to June 2016 under the guidance and supervision of Prof **Dr. A. Arjunan M.D**., Professor Department of Pathology, Coimbatore Medical College.

This dissertation is submitted to The Tamilnadu Dr.MGR Medical University, Chennai towards the partial fulfilment of the requirement for the award of M.D., Degree (Branch III) in Pathology. I have not submitted this dissertation on any previous occasion to any University for the award of any Degree.

Place: Coimbatore

Date: **Dr.LEELAVATHY G**

CERTIFICATE

This is to certify that the dissertation entitled **"THE BETHESDA SYSTEM OF REPORTING THYROID CYTOPATHOLOGY AND ITS HISTOPATHOLOGICAL CORRELATION"** is a record of bonafide work done by **Dr. Leelavathy G** in the Department of Pathology, Coimbatore Medical College, Coimbatore under the guidance and supervision of **Prof. Dr. A. Arjunan M.D**., Professor, Department of Pathology, Coimbatore Medical College and submitted in partial fulfilment of the requirements for the award of M.D. Degree (Branch III) in Pathology by The Tamilnadu Dr. MGR Medical University, Chennai.

Guide
Dr. A. Arjunan, M.D.,
Professor,
Department of Pathology,
Coimbatore Medical College,
Coimbatore.

Head of the Department
Dr. C.Lalitha, M.D.,
Professor,
Department of Pathology,
Coimbatore Medical College,
Coimbatore.

Dr. A.EDWIN JOE.M.D
The Dean,
Coimbatore Medical College,
Coimbatore.

Coimbatore Medical College

COIMBATORE, TAMILNADU, INDIA - 641 014

(Affiliated to The Tamilnadu Dr. MGR Medical University, Chennai)

ETHICS COMMITTEE

CERTIFICATE

Name of the Candidate : DR. LEELAVATHY.G

Course : M.D. PATHOLOGY

Period of Study : 2014 - 2017

College : COIMBATORE MEDICAL COLLEGE

Dissertation Topic : THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY AND ITS HISTOPATHOLOGICAL CORRELATION.

The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation Proposal is accepted / ~~Not accepted~~ and you are permitted / ~~Not permitted~~ to proceed with the above Study.

DEAN

Coimbatore Medical College & Hospital, Coimbatore

21.7.2015

ACKNOWLEDGEMENT

To begin with, I thank the great Almighty for his blessings in all my activities.

I wish to express my sincere thanks to the honourable Dean, **Dr.A.Edwin Joe MD**., Coimbatore Medical College and Hospital, Coimbatore, for permitting me to conduct this study in this hospital.

I extend my gratefulness and thanks to **Prof. Dr.C.Lalitha MD.,** Professor and Head, Department of Pathology, Coimbatore Medical College for her guidance and support and also for providing all facilities to carry out this study.

I am extremely grateful to my mentor and guide **Prof. Dr.A.Arjunan MD.,** Professor, Department of Pathology, for guiding me and providing valuable suggestions and support to complete the study.

I thank all the Associate professors, Assistant Professors and Tutors of the Department of Pathology for their constant support, encouragement and valuable opinions not only for the thesis work but also throughout my postgraduate period in the institution.

I wish to thank all my colleagues, seniors and juniors for their timely help and encouragement.

I wish to thank Department of General Surgery for their support.

I thank all our lab technicians and staff for their help and cooperation.

I express my sincere thanks to my friend Dr. V. Ram prabhakar MD., for his immense help in the statistical work.

I am also grateful to my husband Dr. G. Thiyagarajan MD., for his encouraging words, and support throughout my study. I specially thank my parents Mr. K.S. Ganesan, Mrs. G. Sakunthala and my beloved sister Mrs.G. Pavithra Thirumurthy BE., and her lovable daughter Mullaii Thirumurthy.

It would not be complete without thanking my in-laws, and friends for their tireless support throughout this endeavour.

Last but not the least, I thank all the patients who were a part of this study. Without their cooperation the conduct of the study would not have been possible.

Dr.LEELAVATHY G

turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201413253 Md Pathology Leelavat...
Assignment title:	2015-2015 plagiarism
Submission title:	The Bethesda system of reporting...
File name:	lee_thesis_final_edit18.9.16.docx
File size:	314.91K
Page count:	80
Word count:	9,616
Character count:	57,720
Submission date:	19-Sep-2016 01:14AM
Submission ID:	705723990

"THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY AND ITS HISTOPATHOLOGICAL CORRELATION"

Dissertation submitted in

Partial fulfillment of the regulations required for the award of

M.D. DEGREE

In

PATHOLOGY - BRANCH III

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI.

APRIL 2017

turnitin

Class Portfolio | Peer Review | My Grades | Discussion | Calendar

NOW VIEWING: HOME > THE TAMIL NADU DR.M.G.R.MEDICAL UTY 2015-16 EXAMINATIONS

Welcome to your new class homepage! From the class homepage you can see all your assignments for your class, view additional assignment information, submit your work, and access feedback for your papers.

Hover on any item in the class homepage for more information.

Class Homepage

This is your class homepage. To submit to an assignment click on the "Submit" button to the right of the assignment name. If the Submit button is grayed out, no submissions can be made to the assignment. If resubmissions are allowed the submit button will read "Resubmit" after you make your first submission to the assignment. To view the paper you have submitted, click the "View" button. Once the assignment's post date has passed, you will also be able to view the feedback left on your paper by clicking the "View" button.

Assignment Inbox: The Tamil Nadu Dr.M.G.R.Medical Uty 2015-16 Examinations

	Info	Dates	Similarity	
2015-2015 plagiarism	ⓘ	Start 23-Nov-2015 2:27PM Due 07-Nov-2016 11:59PM Post 01-Dec-2015 12:00AM	10%	Resubmit View

CONTENTS

LIST OF TABLES

LIST OF CHARTS

LIST OF FIGURES

Introduction

INTRODUCTION

Fine needle aspiration cytology (FNAC), considered one of the initial diagnostic investigation in the evaluation of thyroid lesions. The easily available screening test is FNAC. It can effectively categorise patients with neoplastic and non neoplastic thyroid nodules as whether they require surgery or not. Due to lack of standardized system for reporting thyroid lesions in cytology, interpretation of cytology of thyroid reports was difficult for the refering clinicians. To overcome this in year 2007, the National Cancer Institute (NCI) in Bethesda, organised a thyroid fine needle aspiration state of science conference . In the conference an initiative was taken to publish atlas and various guidelines by using a uniform nomenclature in the interpretation of the thyroid fine needle aspirates, known as "The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)". This atlas describes six diagnostic categories of lesions. Non diagnostic/Unsatisfactory is category I, Benign is category II, Atypical Follicular Lesion of Undetermined Significance(AFLUS) is categorised as category III, Suspicious for Follicular Neoplasm comes under category IV, suspicious for malignancy is classified as category VI and malignant lesions come under category VI. Every diagnostic category has it's own risk of malignancy, thereby influencing the management protocol.

Aim & Objectives

AIM OF STUDY

The present study aims at classifying the thyroid fine needle aspirations based on the Bethesda system for reporting thyroid cytopathology and to compare the results with histopathology whereever surgery was done.

OBJECTIVES

I. To analyse thyroid cytology through The Bethesda System for reporting thyroid cytopathology.

II. To analyse the distribution of lesions under various diagnostic categories and subtypes.

III. To analyse whether cytolopathological findings correlated with the histopathological diagnosis.

Review of Literature

REVIEW OF LITERATURE

Embryology of the Thyroid :

The Thyroid, embryologically originates as proliferation of epithelium in pharyngeal floor, inbetween tuberculum impar and copula, which is later represented through foramen caecum . Lately the thyroid descends as a diverticulum which is bilobed in front of the pharyngeal gut . During this migration, the thyroid through the thyroglossal duct attached to the tongue which disappears.[1]

As the thyroid develops, it migrates caudally anterior to hyoid and larynx. Finally in 7th week it is anterior to trachea and it has two lobes which are located laterally and connected with isthmus. The thyroid starts producing hormone by 3rd month, when follicles containing colloid are apparent. Follicular cells synthesise colloid which contain thyroid hormones namely triiodothyronine and the thyroxine. The source of Calcitonin are the C cells which is also known as parafollicular cells.[1]

Thyroid Gland:

The Thyroid contains two lobes which are oval and symmetrical and situated on either side of lower portion of the thyroid cartilage and the tracheal rings. The two lobes of thyroid are interconnected to each other through isthmus, and seen extending from 2^{nd} to 4^{th} tracheal rings. The lateral thyroid lobes have lobules which has about twenty to forty thyroid follicles in a background of well vascularised connective tissue. Histologically, the follicles are round and are lined by cells which are cuboidal and have round regular nucleus. Colloid has thyroglobulin . The Parafollicular cells are also known as C cells, and they are functionally and topographically different from follicular cells. C cells are large, triangular and has clear cytoplasm. They are the source of Calcitonin. The other cell which is less commonly seen is called as the Hurthle cell, which is also called as the oncocytic cell, oxyphil cell, or Askanazy cell. The Hurthle cell is modified follicular cell and has eosinophilic cytoplasm with abundance of mitochondria which is visible in the electron microscope. [2]

FNAC of thyroid gland:

The Fine needle aspiration of thyroid must follow the usual guidelines which is followed for other organs. For thyroid FNA 21- to 26 gauge sized needles are preferred.[3] To obtain an optimal yield, the patient is asked to lie supine with extension of the neck. Thyroid palpated when patient is instructed to swallow. The area of interest is selected, and the overlying skin is cleansed with

spirit. While doing aspiration patient must be immobile. Thyroid is immobilized against tracheal rings with the help of one hand and the aspiration is done swiftly and gently by mobilizing the needle to and fro many times for minimal distance, while maintaining a negative pressure using a 20 ml syringe. The movement is done till blood is seen in needle hub.[4] According to the type and nature of the thyroid lesion the required aspirations can be done. In lesions which are smaller than 3 cm in size 1-4 aspirations are enough. In bigger lesions 4 to 8 aspirations is needed to decrease false-negative interpretations.[5] The aspirations in the central zones of the lesions are not recommended as they have degenerative changes. In patients presenting with multinodular goiter, aspirations from various nodules must be done. In cystic lesions the content must be aspirated and thyroid must be palpated for any remaining nodules or lesions. The aspirated contents of a cyst also studied.

The cytological features of the normal thyroid are:

• Scant bloody aspirate

• Follicular cells may be either dispersed or arranged in small groups

• Bare nuclei may be present resembling normal lymphocytes

• Colloid may be scant

The Follicular cells have pale cytoplasm with central oval to round nucleus with fine chromatin which is granular and with 1-2 small nucleoli. The colloid appears pink with hematoxylin and eosin staining, gray-green with Pap stain and red to violet colour in May grunwald giemsa (MGG) stain.[6]

"The Bethesda System of Reporting Thyroid Cytopathology" :

Literature shows many classification schemes recommended for thyroid fine needle aspirations reporting. Each individual classification was based on the individual's experience or institution's experience. There was no uniform, standardised and internationally recognized system for reporting the thyroid FNAs. This led to confusion and discordance between the clinicians and the pathologists in interpretation of thyroid cytopathology reports.

The various classification schemes adopted by different societies and suggested by several authors include the Papanicolaou Society of Cytopathology in the year 1997, [7] the American Thyroid Association(ATA) in the year 2006,[8] the American Association of Clinical Endocrinologists and the Associazione Medici Endocrinologi in the year 2006,[9] the Royal College of Physician - British Thyroid Association and the Italian Society of Anatomic pathology and Cytopathology (SIAPEC).

In the year 2007, 'the National Cancer Institute (NCI)' of United states in Bethesda organized a conference and came with a system with standarized nomenclature for reporting thyroid fine needle aspirations ,which is called as "The Bethesda System of Reporting Thyroid Cytopathology". The Bethesda conference was preceeded by an online forum along with panel discussion, and is a great achievement in arriving at a uniform, internationally accepted system in interpretation of FNAs of thyroid. The Bethesda classification is a six tiered system.

"THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY, RECOMMENDED DIAGNOSTIC CATEGORIES":

I. "Non diagnostic or unsatisfactory":

- Cyst fluid
- Acellular specimen
- Others (blood, clotting artifacts etc)

II. "Benign":

- Consistent with a "benign follicular nodule" (adenomatoid goiter, colloid goiter)
- Consistent with "lymphocytic (Hashimoto) thyroiditis"
- Consistent with "granulomatous (subacute) thyroiditis"
- Other

III. "Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance":

IV. "Follicular Neoplasm or Suspicious for a Follicular Neoplasm":

Specified whether Hurthle cell variant

V. "Suspicious for Malignancy":

- Suspicious for 'Papillary carcinoma of thyroid'.
- Suspicious for 'Medullary carcinoma'.
- Suspicious for 'Metastatic carcinoma'.
- Suspicious for 'Lymphoma'.
- Others

VI. "Malignant":

- Papillary carcinoma of thyroid
- Poorly differentiated carcinoma of thyroid
- Medullary carcinoma of thyroid
- Undifferentiated (anaplastic) carcinoma of thyroid
- Squamous cell carcinoma
- Carcinoma with mixed features (specify)
- Metastatic carcinoma
- Non – Hodgkin lymphoma
- Others"[10]

"The Bethesda system also describes about the malignancy chance in each category and suggests management for the patients in each category. The malignancy risk for benign lesions is 0-3% and those cases are suggested to undergo clinical follow up. The malignancy risk for category III is 5- 15%, repeat FNA is the recommended management. For category IV the risk of malignancy is 15 – 30%. Surgical lobectomy is recommended management. Category V has malignancy risk of 60% to 75% , lobectomy or near total thyroidectomy is recommended. In case of category VI the malignancy risk ranges from 97-99%. Near total thyroidectomy is the recommended management for the malignancy category".[10]

1) "Nondiagnostic or Unsatisfactory":

The smear is called "Nondiagnostic" or "Unsatisfactory" when it doesnot fulfil the criteria which is necessary to say as adequate sample.

Adequacy criteria:

The thyroid aspiration material is considered to be adequate when it has atleast six groups containing follicular cells which are well stained and without any distortion. Each group must have minimum ten cells per slide. Exceptions for the criteria considered in the following conditions:

1. "*Solid thyroid nodules with cytologic atypia"*: Smears with considerable amount of atypical features is not considered non diagnostic /unsatisfactory irrespective of the number of follicular cells. It is important to report the atypia.[10]

2. "*Solid thyroid nodules having inflammation"*: The thyroid lesions in patients suffering from autoimmune thyroiditis, abscess of thyroid or granulomatous inflammation of thyroid, may have inflammatory cells only. Those cases must be categorized under benign and not under non diagnostic category. The adequate number of follicular cells is not necessary here.[10]

3. "*Colloid nodules":* Smears with thick abundant colloid are categorized as satisfactory samples and classified as benign lesions. Here also the number of follicular cells for adequacy is not a must if colloid is predominant.[10]

"Nondiagnostic category":

The following scenarios describe cases of Nondiagnostic category:

1. Less than six clusters of well-preserved and stained follicular cell groups with each containing ten cells.[10]
2. Follicular cells which are poorly preserved or poorly stained
3. Smears with only cyst fluid, containing histiocytes or without them, and below six clusters of benign follicular cells with atleast 10 cells in each group.[10]

Smears must be adequate to decrease the false negative interpretations. The ability to obtain adequate sample depends on lesion's nature. Solid nodules with cytological atypia must be taken as adequate for evaluation and interpreted as abnormal. Even one cluster containing follicular cells having

cytomorphological features diagnostic for papillary carcinoma must be reported as such if clinical condition permits and not as non diagnostic even though they are scantly cellular . A sample containing cyst fluid and macrophages, must be reported as non diagnostic which is category I with a note saying cyst fluid only due to the risk of missing a cystic papillary carcinoma.

If aspiration involves adjacent sternocleidomastoid muscle or trachea, they must be reported as non diagnostic/ unsatisfactory.

Nodules initially interpreted as unsatisfactory must be reaspirated, after an interval of three months, to overcome false positive interpretations because of reactive changes.[11] With Ultrasound guidance repeat aspiration recommended for solid nodules. Reaspiration helps in achieving a diagnostic interpretation approximately in 60% of cases.[12,13] Most of the nodules on follow up are benign.[14,15]For cystic lesions, re-aspiration done when the ultrasonography features are abnormal.

2) **BENIGN** :

Thyroid FNA gains relevance because of its ability to diagnose benign thyroid lesions, thereby avoiding unwanted surgical interventions. Most of the thyroid lesions are benign, so the commonest thyroid FNA result is benign (65%).[16]Benign cytopathology has a lower malignancy risk,[17]and the patients are followed clinically and radiologically regularly.

Sub-classifications :

(i) "Benign follicular nodules"

(ii) "Thyroiditis"

(iii) Other uncommon lesions.

"Nodular goiter (NG)" is one of prevalent thyroid pathology undergoing FNA, and "lymphocytic or Hashimoto's thyroiditis" is the frequent cause for thyroiditis.[10] Follicular nodules which are benign have varying colloid quantity, benign thyroid follicular cells, macrophages and Hurthle cells .

Definition :

"Benign follicular nodule(BFN)" diagnosis must meet the adequacy criteria and must have predominant amount of colloid and thyroid follicular cells which are benign appearing.[10]

Criteria

- Specimens must have scant to moderate cellularity.
- Colloid may be thick, shiny, and have golden yellow appearance. It is dark blue or violet magenta in 'Romanowsky stain' and green to orangish pink in 'Papanicolaou stain'.[10]
- Colloid can be thin or thick, when thin gives crazy pavement appearance and when thick it has a hyaline appearance with cracks.[10]
- Follicular thyroid cells are in macrofollicles or honeycomb like appearance.[10] Microfolliculi can also be seen rarely.

- Follicular cells have delicate cytoplasm which is scant to moderate, round dark nucleus and fine chromatin. Minimal nuclear atypia, crowding and overlapping can also be seen.
- Hurthle cells, macrophages, squamoid, spindle cells focally can be seen.

BFN cytology varies from colloid goiter with abundant colloid and less cellularity to adenomatous goiter having more cellularity and lesser amount of colloid.[18,19] The occurence of honeycomb clusters of thyroid follicular cells, along with Hurthle cells, and predominantly colloid is characteristic for BFN.

Thin colloid resembles serum in blood contaminated specimens. But the presence of cracking artifact in colloid, and its nature to cover the thyroid follicular cells helps in differentiating it from serum which gather slide edges and surrounding blood platelets or fibrin.

Smears with predominantly colloid and scanty follicular cells, are interpreted as BFNs and interpreted as 'colloid nodule or consistent with colloid nodule'.[10]These cases, colloid and serum must be differentiated as it covers substantial amount of surface of slide.

Thyroid cysts containing scant follicular cells are reported Nondiagnostic" or "Unsatisfactory," and commented as "cyst fluid only" .

Moderately cellular BFNs should not be interpreted as "Follicular neoplasm/Suspicious for a follicular neoplasm (FN/SFN)" depending on the

quantity of cellularity alone. Predominant follicular cells with crowding of cells, overlapping and arranged as microfollicles are characteristic of SFN smears.[20]

Benign lesions containing microfollicles in lesser proportion and predominantly macrofollicles are diagnosed benign follicular neoplasm. Macrofollicles differ in size. Microfollicle must have features of crowding of follicular cells and overlapping.

The Hurthle cells occurrence as such is not an indication for diagnosing the lesion as "Follicular neoplasm, Hurthle cell type/ Suspicious for a follicular neoplasm, Hurthle cell type (FNHCT/SFNHCT)." Hurthle cells can occur as a minor component or as a predominant component of a BFN, with anisonucleosis and hyperchromatic nuclei. The interpretation of "FNHCT/SFNHCT" are done for lesions with exclusive hurthle cells.[20]

FNA cannot differentiate nodular goiter from colloid predominant macrofollicular adenoma, so they are interpreted as benign follicular lesion. If a smear contain even a minimal cluster of follicular cells showing nuclear characteristic features favouring papillary thyroid carcinoma they must be given "Suspicious for malignancy" or "Atypia of Undetermined Significance (AUS)", depending on amount of atypia.[21]

Graves' Disease

Graves' disease is an autoimmune disease affecting thyroid. It affects middle aged women and patients present with hyperthyroidism. The cytomorphological findings are not characteristic and must be clinically

correlated with clinical features.[22] There can be cellular smears with more colloid and follicular cells in variable numbers resembling other benign lesions. Background can occasionally show lymphocytes and oncocytes. Follicular cells can be flat sheets or non cohesive clusters, with abundant amount of cytoplasm . Nuclei are large, vesicular and have prominent nucleoli. Distinctive flame cells show vacuoles in margins of cytoplasm with fraying of edges of cytoplasm.[22] Flame cells are not characteristic of Grave's disease but also occur in follicular lesions of thyroid and Papillary carcinoma of thyroid. Follicular cells can display clearing of chromatin focally and grooves in the nuclei.

Treated GD may show microfollicles predominantly, with overlapping of nuclei, crowding and atypia. These changes must not be over-interpreted as malignant or neoplastic, and enquired for prior radioactive iodine therapy.[22]

"Lymphocytic (Hashimoto´s)Thyroiditis(LT)":

Definition:

"Consistent with lymphocytic (Hashimoto's) thyroiditis" term must be used for cytology smears with polymorphic population of lymphoid cells and containing Hurthle cells.[23]

Criteria for diagnosis:

Hypercellular smears usually, but scant cellularity may also occur due to fibrosis of the thyroid gland or dilution due to peripheral blood . For reporting lymphocytic thyroiditis adequacy criteria is not mandatory.[10]

The polymorphous population of lymphoid cells may contain small mature looking lymphocytes, large reactive lymphoid cells with occasional plasma cells. The lymphoid cells are seen in the background or seen impinging on the follicular cell clusters. Lymphoid follicles and aggregates of histiocytes also seen. Hurthle cells can occur singly or in clusters. Hurthle cells have large granular cytoplasm, nuclei which is enlarged with prominent nucleoli. Anisonucleosis, mild nuclear atypia scattered nuclear clearing and grooves can occasionally be seen in hurthle cells.

"Granulomatous (subacute, de Quervain´s)Thyroiditis":

"Granulomatous (subacute, de Quervain's) thyroiditis" is inflammation of thyroid , diagnosed clinically. Fine needle aspiration done for nodules in this condition which are suspicious. If granulomas are absent the cytologic findings are nonspecific.

Criteria:

According to stage of disease cellularity varies. Granulomas with epitheliod histiocytes are seen with giant cells which have multiple nuclei. In initial stage neutrophils and eosinophils occur as in acute thyroiditis.[25]The smears are hypocellular in the later stages. They contain giant cells engulfing the colloid with histiocytes, lymphocytes, and degenerated thyroid follicular cells.[25]In the involutional stage, there may be absence of giant cells and inflammatory cells . Occasionally some specimens may be unsatisfactory.

“Acute Thyroiditis”:

Acute thyroiditis is infectious disorder of thyroid which is uncommon, seen prevalently in subjects who are immunocompromised.

Criteria:

Neutrophils are seen with necrosis and fibrin material. Macrophages, and blood are also seen. Follicular cells which are reactive with scant colloid seen. Bacteria or fungi can be seen mainly in immunocompromised. Additional investigations like cultures along with special stains to demonstrate microbials may be useful here.

“Riedel´s Thyroiditis/ Riedel’s Disease”:

It is one of the uncommon variant of thyroiditis associated with extensive fibrosis involving the thyroid gland and also with extension into the surrounding soft tissues located in the region of neck.

Criteria:

The Thyroid gland is firm due to fibrosis. The smears are acellular. The presence of occasional strands of collagen bundles and spindle shaped cells which are bland also seen with inflammatory cells of chronic type. Follicular cells, colloid are not seen.

Patients suffering from lymphocytic thyroiditis, with predominant population of lymphoid cells or hurthle cells raises the occurence of either lymphoma or Hurthle cell neoplasm.[26,27] The predominant occurrence of monomorphic lymphoid cells raises the suspicion of lymphoma and it must be

confirmed with flow cytometry. The interpretation of "FNHCT/SFNHCT" considered in cases without lymphocytes. The follicular cells of thyroid or the Hurthle cells sometimes show occasional reactive features and atypia minimally, including nuclear enlargement, grooves in nuclei, and clearing of chromatin.[26] Hence, with caution the diagnosis of papillary carcinoma be made when there is cytomorphological features of Lymphocytic Thyroiditis. In these cases Non diagnostic, "Atypia of undetermined significance" or "Suspicious for malignancy" made because of nuclear features. Occasionally stripped nuclei of follicular cell mistaken for lymphocytes, so scant cytoplasm surrounding lymphocytes taken into account to overcome misdiagnosis of Lymphocytic thyroiditis. The diagnosis of Lymphocytic thyroiditis on liquid based cytology is difficult, because of decrease or absence of chronic inflammatory cells in the background.[28,29,30] The lymphoid cells are evenly distributed in the background in liquid based cytology. As the liquid based cytology have advantage of eliminating RBCs, it relatively has more lymphocytes, so these must not be misdiagnosed as Lymphocytic thyroiditis. In Lymphocytic thyroiditis, there is marked increase in the percentage of lymphoid cells than other inflammatory cells. In liquid based cytology, Hurthle cells are with irregular nuclei occassionally. Cytomorphological features are not specific for acute or subacute or Riedel's thyroiditis and they can overlap between some Lymphocytic thyroiditis cases.[23,25]A thorough meticulous examination of FNA material done

to exclude associated malignancy like fibrosing anaplastic carcinoma or sclerosing lymphoma.

Management:

Patients having benign thyroid cytological diagnosis must be kept under clinical and radiological follow up every 6 to18 months for at least three to five years following first benign diagnosis. Repeat of the needle aspiration is suggested for thyroid lesions which show significant change in size or ultrasonography abnormalities with margins which are irregular, micro calcifications, or increase in vasculature within nodules and hypoechogenicity of solid areas.[31]The calculation for risk of malignancy for cytomorphologically benign thyroid lesions is often difficult because only limited patients undergo surgery for non neoplastic lesions . Surgery is recommended for nodules, with larger size, and with symptoms, or present with worrisome clinical, sonographic characteristics, or have contralateral malignancy.

(III) "Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance":

Definition:

The "Atypia of Undetermined Significance" category consists of specimens with follicular cells or lymphoid cells with atypia, but insufficient to categorise under "suspicious for a follicular neoplasm" or "suspicious for malignancy", or as malignant lesion. However, the atypia is prevalent than benign lesions. The factors causing uncertainty are scant cellularity and presence

of blood or blood clots. The interpretation of "Follicular Lesion of Undetermined Significance (FLUS)" made when follicular cells show atypia.

The AUS interpretation is appropriate in the following:

1. When there is presence of microfollicles prominently, but inadequate for "Follicular Neoplasm/Suspicious for Follicular Neoplasm."
2. When Hurthle cells are predominant.
3. In presence of air drying artifact or clotting artifact.
4. A cellular sample with Hurthle cells exclusively, but clinically benign Hurthle cell containing nodule:
    a. 'Hashimoto's thyroiditis'
    b. 'Multinodular goiter'
5. Focal presence of characteristic nuclear features of papillary carcinoma in a predominantly benign sample
6. When there are cyst-lining cells which show atypical features like nuclear grooves, nucleoli prominence, intranuclear inclusions in a predominant benign looking smear.
7. A small proportion of follicular cells with large nuclei and prominent nucleoli.

    i. With positive history of treatment with radioactive iodine or carbimazole or any other pharmaceutical drugs

ii. Involutional changes in cystic degeneration or hemorrhage

8. When lymphoid infiltration with atypia, but amount is inadequate to categorise it as "suspicious for malignancy."

About approximately 3–18% of thyroid cases are categorized into AUS category. Despite specific criteria, it has only fair reproducibility. The amount of "AUS" must be around 7% among total thyroid cytology interpretations. AUS considered category of last resort and it use indiscriminately must be avoided. When clonality studies are unavailable, it is appropriate to recommend aspiration again for investigation like flow cytometry.[10]

Management :

The management for AUS diagnosis is to correlate clinically and repeat FNAC.[31,33] A repeated FNA usually provides definitive diagnosis. About 20 to 25% nodules again reported as AUS.[33,34] The malignancy risk in this category is difficult to assess because only few cases have surgical follow-up.[33,35] After evaluating all AUS nodules the risk of malignancy ranges from 5–15%.

(IV) Follicular Neoplasm/Suspicious for a Follicular Neoplasm

In the past different terminologies were used to describe lesions which were suspicious of Follicular neoplasm like "follicular lesion," "follicular proliferation," and "indeterminate" to the more definitive terms like "rule

out/suggestive of/suspicious for follicular neoplasm". In "The Bethesda system", the terms "Follicular Neoplasm" and "Suspicious for Follicular neoplasm" are same. "Suspicious for a follicular neoplasm (SFN)" is preferred term than "Follicular neoplasm (FN)" due to the presence of a good number of cases approximately around 35% which meet criteria described are just hyperplastic proliferations occurring in nodular goiter and not neoplasms.[35-38]

" FN and SFN" preferred than "suspicious for follicular carcinoma" as in FNA it is not possible to distinguish an adenoma from carcinoma. "Follicular neoplasm" or "Suspicious for a follicular neoplasm" means a cellular aspirate with follicular cells in microfollicles and with cell crowding. The smears with characteristic nuclear features suggesting papillary carcinoma thyroid are not included here.

Criteria:

- Smears with moderate or marked cellularity
- Alteration of follicular cell pattern showing crowding, microfollicle formation, and singly scattered cells
- Follicular cells are normal or large in size
- Scant to moderate amount of cytoplasm

- Nuclei round and showing hyperchromasia and have inconspicuous nucleoli
- Nuclear atypia occasionally seen
- Colloid scant or absent

The diagnostic feature for “FN/SFN” is occurence of follicular cells with marked architectural change . It may be crowded and overlapping follicular cells or arranged as microfollicles. The “microfollicle” term corresponds to crowded follicular cells and below 15 follicular cells per cluster, which occur in circle which is upto 2/3rd complete.[39] Colloid seen inside microfollicle. Microfollicles are uniform. Follicular cells may form “trabeculae”. Macrofollicles can also be seen in FN/SFN.

Though mostly a cellular smear, cellularity by itself is not sufficient to make a diagnosis of FN/SFN. Cellular smear with majority of macrofollicles are interpreted as benign. Similarly a smear with sparse cellularity, but with predominant microfollicular pattern is reported as AUS. If nuclear features of papillary carcinoma are noted, then it is designated as “MALIGNANT,

Papillary thyroid carcinoma” which is category VI or as category V “SUSPICIOUS FOR MALIGNANCY, suspicious for Papillary thyroid carcinoma,” owing to degree and amount of cytologic features. Parathyroid

adenomas have cells similar to follicular cells which show crowding and overlapping so it can be misinterpreted as FN/SFN.

65–85% of FN/SFN are neoplastic when followed up histopathologically. The rate of malignancy in this category is 12–32% and many are Papillary thyroid carcinoma than Follicular carcinoma (27–68%).[40]

Management :

The Management recommended for this category is FN/SFN is surgery like hemithyroidectomy or surgical lobectomy.

(b) "Follicular Neoplasm, Hurthle CellType/Suspicious for a Follicular Neoplasm, Hurthle Cell Type":

The Hurthle cell (also called as Askanazy cell or as an oncocyte or as an oxyphilic cell) is a thyroid follicular cell with abundant granular cytoplasm. Hurthle cells have enlarged round to oval nucleus with prominent nucleolus. According to "World Health Organization (WHO)" Hurthle cell adenoma, Hurthle cell carcinoma are considered variants of follicular adenoma and carcinoma respectively [41] but in "The Bethesda System" , "suspicious for Hurthle cell neoplasm" are distinguished and categorized separately from the specimens which are considered as "suspicious for a follicular neoplasm" mainly because of the following reasons:

(1) morphologic difference in cytology seen between them and

(2) due to the datas which show the genetic difference between the follicular and Hurthle cell carcinomas.[21]For example, the PAX8-PPAR gamma rearrangement noted in 26 to 53% of Follicular carcinoma of thyroid but not seen in Hurthle cell carcinomas.[42,43]

"Suspicious for a follicular neoplasm, Hurthle cell type (SFNHCT)" term is preferred over the term "Follicular neoplasm, Hurthle cell type (FNHCT)" because about 16 to 25% of cases are hyperplasia of Hurthle cells and not neoplasms. Hurthle cell carcinomas rare and they constitute about 15 to 20 % of the Follicular carcinomas.

"Follicular neoplasm, Hurthle cell type" or "Suspicious for a follicular neoplasm, Hurthle cell type" indicates cellular smear with Hurthle cells exclusively. Oxyphilic cells which show nuclear morphology characteristic of Papillary carcinoma are not included .

(V) "Suspicious For Malignancy (SFM)":

SFM category predominantly have cases that are "Suspicious for Papillary thyroid carcinoma (PTC)".The cases in "Suspicious for PTC" category are between 2.4% to 7.9%.[16,28,33,44]. This category used cautiously for appropriate management of patients and allows for other management modalities (surgical lobectomy including intra operative frozen section) prior to definitive surgery

like total thyroidectomy. It is mandatory to separate "suspicious" category from "malignant" category to maintain positive predictive value (PPV) of malignancy category without compromising overall sensitivity of the procedure.

Definition

"Suspicious for Malignancy (SFM)" category specimens have morphology with strong suspicion for malignancy, but not sufficient for definitive diagnosis. "Suspicious for a follicular neoplasm" or "suspicious for Hurthle cell neoplasm" which belong to category IV are excluded from this category. The PPV of category V is 55 to 85%.[45]

Criteria:

Suspicious for Papillary Carcinoma:

Pattern A ("Patchy Nuclear Changes Pattern"):

Cellularity of the smears ranges from moderate cellularity to high cellularity with follicular cells in macrofollicles, along with cells having large pale nuclei showing grooves, irregular nuclear membrane and molding. Intranuclear inclusions are occasional.

Pattern B ("Incomplete Nuclear Changes Pattern"):

Cellularity of the smear varies from sparse to moderate or high, with mild to moderate degree of nuclear enlargement and pale nuclei. Grooves in nuclei occur, though irregular nuclear membrane and molding rarely seen.

Pattern C (“Sparsely Cellular Specimen Pattern”):

Scantly cellular smear eventhough many features of PTC are present.

Pattern D (“Cystic Degeneration Pattern”):

Here features of cystic degeneration and follicular cells in scattered groups and sheets with enlarged palor nuclei and grooves seen, INCIs rarely seen. Occasionally cells which are bigger and atypical and show nuclear enlargement and “histiocytoid” cells having abundant vacuolated cytoplasm also occur.

Suspicious for Medullary Carcinoma

Cellularity of smear ranges from sparse to moderate with uniform discohesive cells which are small to medium in size with high nuclear/cytoplasmic (N/C) ratio**.** The Nucleus is eccentrically placed and have smudged chromatin and without cytoplasmic granules. Little fragments of amorphous material namely colloid or amyloid can be seen.

Suspicious for Lymphoma:

A cellular sample with many monomorphous small to medium sized lymphoid cells.

Or

A sparsely cellular smear with atypical lymphoid cells.

The nuclear morphology of papillary thyroid carcinoma is also seen in lymphocytic thyroiditis, cystic degeneration, radioiodine and with carbimazole therapy. Variants of PTC also pose diagnostic difficulties.

Management of these cases include surgical resection. For tumours >4 cm total thyroidectomy is preferred as risk of malignancy increases as size increases.

Additional serologic or immunohistochemical investigations, are not necessary in "suspicious for papillary thyroid carcinoma," cases but useful in "suspicious for MTC" and in the category of "suspicious for lymphoma." Increased serum calcitonin levels and repeated aspiration with strong immunoreaction for immunohistochemical markers like Chromogranin, Synaptophysin and Calcitonin can change the interpretation of "suspicious for MTC" to definitive malignancy. FNAC is repeated for obtaining sample for flow cytometric study which will give definite diagnosis in patients with interpretation of "suspicious for lymphoma".

(VI) Malignant

Papillary thyroid carcinoma is one of the most prevalent malignant thyroid carcinoma(80%) affecting all ages with more prevalence in 3^{rd} to 4^{th} decade. Male to Female ratio is 1:3. Risk factors are irradiation to head and neck in younger days, ionizing radiation and also hereditary factors and hyperplastic nodules. PTC may present as nodule or diagnosed incidentally or rarely present

with lymph node metastasis. Malignant thyroid FNAC report constitutes about 4 to 8% of all the thyroid cytology,[16,33,35] the major proportion is Papillary carcinomas. Conventional Papillary carcinoma have characteristic papillae which are lined by follicular cells which are cuboidal in shape to low columnar with characteristic nuclear morphology in histopathology.

If diagnosis of Papillary carcinoma made definitely through FNA, nearly 96–100% are PTC on histological follow-up.[33,35,44-46]

Papillary Thyroid Carcinoma:

Definition

PTC is a malignant thyroid follicular epithelial tumor which show characteristic nuclear morphology. Papillary architecture as such is not mandatory for diagnosis.

Criteria (for conventional PTC, all types and Variants):

Follicular cells arranged in papillary architecture or syncytial monolayer sheets.

The Malignant follicular cells show the following characteristic nuclear morphology:

- Nuclear enlargement
- Oval or irregular nuclei with occasional molding
- Longitudinal grooves in nuclei
- Intranuclear cytoplasmic pseudoinclusions
- Palor nuclei with powdery chromatin (“Orphan Annie” nuclei)

- Solitary or multiple micronucleoli
- Psammoma body.
- Multinucleate giant cells
- Stringy colloid, ropy or "bubble-gum" like colloid.
- Hurthle cell metaplasia and squamous metaplasia can also be seen.

In cytology the malignant follicular cells are arranged in monolayered sheets showing crowding, overlapping and molding of the nucleus. Nuclear crowding, overlapping, and molding are characteristic findings to differentiate from benign follicular cells. Cells of Papillary carcinoma vary in size and shape.[47]They have well defined cell border and variable quantity of cytoplasm.

Nuclear features are defining ones in the diagnosis of PTC. They can be round or oval, with highly irregular contour, and pale powdery chromatin unlike dark coarse chromatin of benign follicular cells. The pallor of nucleus is more evident in formalin-fixed tissue, which gives the appearance of Orphan Annie nuclei. Intranuclear inclusions occur in 50 to 100% cases, but they are not specific for PTC and occur in Medullary carcinoma of thyroid, Anaplastic thyroid carcinoma and Poorly differentiated thyroid carcinoma. Very rarely they are also seen in benign thyroid nodules (e.g., follicular adenoma, nodular goiter, and lymphocytic thyroiditis). Nuclear groove is other characteristic feature of PTC .[48] In alcohol fixed and Papanicolaou stained smears nuclear grooves are well visualised. Nuclear grooves are also not specific of papillary carcinoma. Multinucleated giant cells are also a common non specific finding seen in PTC.

Psammoma bodies (PBs) are less frequent in cytology than in histopathology. The positive predictive value of Psammoma body alone is 50%, but when associated with other cytomorphologic findings of PTC, positive predictive value is 100%.[49]

Variants of Papillary Thyroid Carcinoma

PTC variants also have the same characteristic nuclear morphology of PTC but differs in architectural arrangement, cytoplasmic findings and background. Colloid and lymphoplasmacytic infiltrate also differ. Prognosis of PTC variants also vary, subtyping of papillary carcinoma is impossible and not mandatory through FNA.

Management :

The "American Thyroid Association" recommends total thyroidectomy or near total thyroidectomy in the following conditions:

i. Larger than 1.5cm malignant nodule
ii. Contralateral nodules
iii. Metastasis
iv. Past history of irradiation
v. Family history of thyroid cancer.[50]
vi. Older age (>45 years)

Medullary Thyroid carcinoma:

Medullary carcinoma was first described and illustrated by Horn in 1951. It constitutes nearly seven percentage of all thyroid malignancies. It may occur

sporadically or inherited. The inherited types have point mutations of RET proto-oncogene located on the chromosome 10. MTC can occur in all ages but commonly occurs in older adults in 5th decade. It is an aggressive tumour with hematogenous and lymphatic spread.

Definition

"Medullary Thyroid carcinoma is a malignant neoplasm derived from the morphologically similar parafollicular cells of the thyroid gland".[10]

Criteria:

- Moderate to markedly cellular smears.
- Many isolated cells and syncytial clusters seen.
- Plasmacytoid cells seen.
- Neoplastic cells with mild to moderate pleomorphism.
- Rare bizarre giant cells seen.
- Nuclei have eccentric location, with "salt and pepper" chromatin
- Pseudoinclusions in nuclei seen.
- Nuclei can be either binucleated or multinucleated .
- Inconspicuous nucleoli occur.
- Granular cytoplasm seen.
- Amyloid which is present often seen as dense material resembling colloid.

- Cells immunoreactive for calcitonin, chromogranin, CEA, Synaptophysin and Thyroid Transcription Factor-1 but negative for thyroglobulin.

Management:

The recommended management is total thyroidectomy along with lymph node dissection.[47,48] At present no definitive treatment for recurrent disease or metastases. Targeted therapy for against *RET* kinase pathway now is in research.[51]

Poorly differentiated carcinoma

Poorly differentiated thyroid carcinoma is thyroid neoplasm which arises from follicular cell with insular or trabecular pattern. This lacks diagnostic nuclear morphology of Papillary thyroid carcinoma. They have poorly differentiated features like numerous mitotic figures, necrosis and small convoluted nuclei. The neoplastic cells have increased nuclear cytoplasmic ratio and also show nuclear atypia. Apoptosis, mitotic activity and necrosis are usually present.

Poorly differentiated thyroid carcinoma diagnosis in cytology is difficult because of overlapping cytomorphological features with follicular neoplasms and the cytomorphological findings are not specific.

Management

Poorly differentiated carcinoma must be managed aggressively due to their poor prognosis. For stage T 3 and stage T 4 diseases, patient benefit from external beam radiotherapy.

“Undifferentiated (Anaplastic)Carcinoma”:

“Undifferentiated (anaplastic) thyroid carcinoma (UTC)”, also known as “giant and spindle cell carcinoma,” is aggressive thyroid neoplasm. It accounts for not more than 5% of malignant thyroid neoplasms,[52,53] and it has worst prognosis than other well differentiated thyroid carcinoma and poorly differentiated forms.[54]

UTC is high grade neoplasm with epithelioid cells and spindle shaped cells .

Smears are moderately to highly cellular, with cells arranged in variable sized clusters. Neoplastic cells are epithelioid, spindle-shaped, plasmacytoid and rhabdoid. Nuclei are enlarged, irregular and pleomorphic. Chromatin clumping with parachromatin clearing, irregular nucleoli and intranuclear inclusions also seen. Nuclei can also be eccentrically placed and may show multinucleation.

Necrosis, extensive inflammation ,osteoclast-like giant cells are seen occassionally. Neutrophilic infiltration and many abnormal mitotic figures seen.

Tumor cells show focal positivity for Pan-keratin and vimentin and negative for TTF-1 and thyroglobulin.

Management :

Complete surgical resection, including prior radiotherapy and chemotherapy to improve resectability by decreasing tumor size is the recommended treatment.[55,56] Patients who are less than 45 years, small tumors with no extrathyroidal extension or metastases have better prognosis.[53,55,57]

"Squamous Cell Carcinoma of the Thyroid Gland":

Squamous cell carcinoma accounts for < 1% of thyroid neoplasms. It is prevalent in elderly age and have worse prognosis.

FNA smears have large, pleomorphic keratinized cells. Necrosis seen. Differential diagnosis include anaplastic carcinoma and secondary metastases from squamous cell carcinoma.

Metastatic Tumors and Lymphomas

Metastases from remote structures and direct extension from adjacent organs carcinoma are not common but must be recognized in aspirations of thyroid nodules. Rarely metastasis to thyroid may be initial manifestation of malignancy elsewhere.

Metastatic carcinomas may occur either as multiple discrete nodule (< 2mm) or as solitary large nodule in thyroid and diffuse involvement.

The most common secondaries to thyroid are from carcinoma of the lung, mammary gland, skin (mainly melanoma), large intestine and kidney.[58-62]

Lymphoma :

Malignant lymphomas can occur in the thyroid as primary neoplasm or as secondary involvement from systemic disease.[63] Most of the primary lymphomas arising in thyroid are of B cell category. Two third of cases are preceeded by autoimmune thyroiditis. Most Non hodgkins lymphoma of thyroid are DLBCL or extranodal marginal zone lymphomas of B cell category - mucosa associated lymphoid tissue(MALT) lymphoma.

Materials & Methods

MATERIALS AND METHODS

STUDY DESIGN

Cross sectional study

STUDY SETTING

Department of Pathology, Coimbatore Medical College.

DURATION OF STUDY

One year, July 2015 to June 2016

INCLUSION CRITERIA

Fine needle aspiration of patients with thyroid lesions at the Department of Pathology, Coimbatore Medical College who subsequently underwent thyroidectomy at our institution during the study period were included.

EXCLUSION CRITERIA

a. Fine needle aspirations of thyroid without further thyroidectomy
b. Thyroidectomy specimens without previous fine needle aspirations

ETHICAL CLEARANCE

The study was initiated after obtaining clearance from the institutional research and ethics committee. Understandable written informed consent was obtained from the patient.

METHODOLOGY

Study done in Department of Pathology, Coimbatore Medical College. After obtaining detailed clinical history and getting informed consent, the site is cleansed with spirit and fine needle aspiration was done using 21 to 26 gauge needle and 20ml syringe. Aspirate obtained is immediately spread on to a glass slide. One slide is air dried for May Grundwald Giemsa stain and other slide fixed in isopropyl alcohol for 15 minutes. After Alcohol fixation smears are stained with Papanicolaou stain. The smears are examined and cytological diagnosis is made and categorized according to The Bethesda system.

Thyroidectomy specimens are fixed in 10% buffered formalin overnight. Appropriate bits are taken the next day. Processing was done with histokinete, blocks made, sections are cut with Leica microtome in 5 µ thickness. Sections are stained with Hematoxylin and Eosin stain and studied and histopathological diagnosis made.

STUDY VARIABLES

i. FNA diagnosis

ii. Histopathological diagnosis

STATISTICAL ANALYSIS

All the data were entered into Microsoft Excel 2010. Statistical analysis performed using SPSS version 20.0 (statistical package for social sciences). Results were interpreted using tables, bar diagrams and pie charts. Descriptive statistics like mean, median, standard deviation, and range were also calculated.

Observations and Results

OBSERVATION AND RESULTS

In the study period from July 2015 to June 2016 of 12 months, 143 cases of thyroid fine needle aspirations were collected and categorized according to The Bethesda system of reporting thyroid cytopathology, and it was correlated with the histopathological diagnosis.

AGE : Patients with thyroid lesions in this study ranged from 9 years to 80 years.

TABLE-1: Distribution of patients according to age (N=143)

Age	Number	Percent (%)
1-10	1	0.69
11-20	7	4.89
21-30	23	16.08
31-40	50	34.96
41-50	39	27.27
51-60	12	8.39
61-70	8	5.59
71-80	3	2.09
Total	143	100

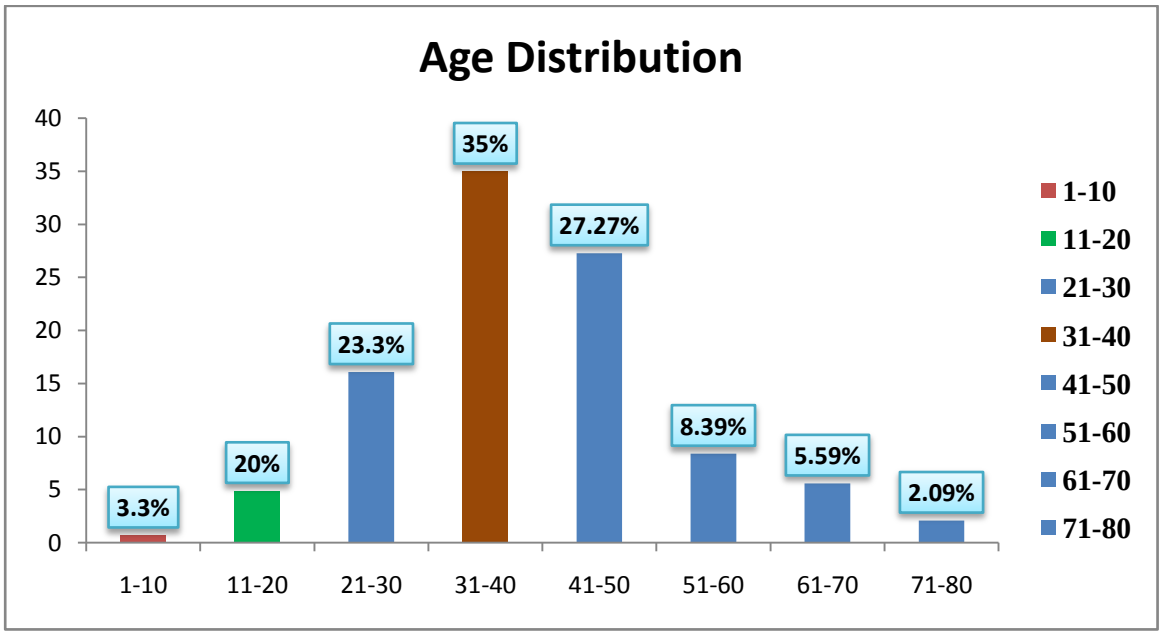
Mean ± SD= 32.77± 7.284

Median (IQR) =32.5(9-80)

Comments:

Major proportion of the patients (35%) belonged to age group of 31-40 years

Chart 1 : Percentage distribution of the sample according to age



SEX:

Out of the 143 patients with thyroid lesions 108 were females and 35 were males. Female to male ratio is 3:1. The youngest patient was 9 years old female child and the eldest was 80 year old female**.**

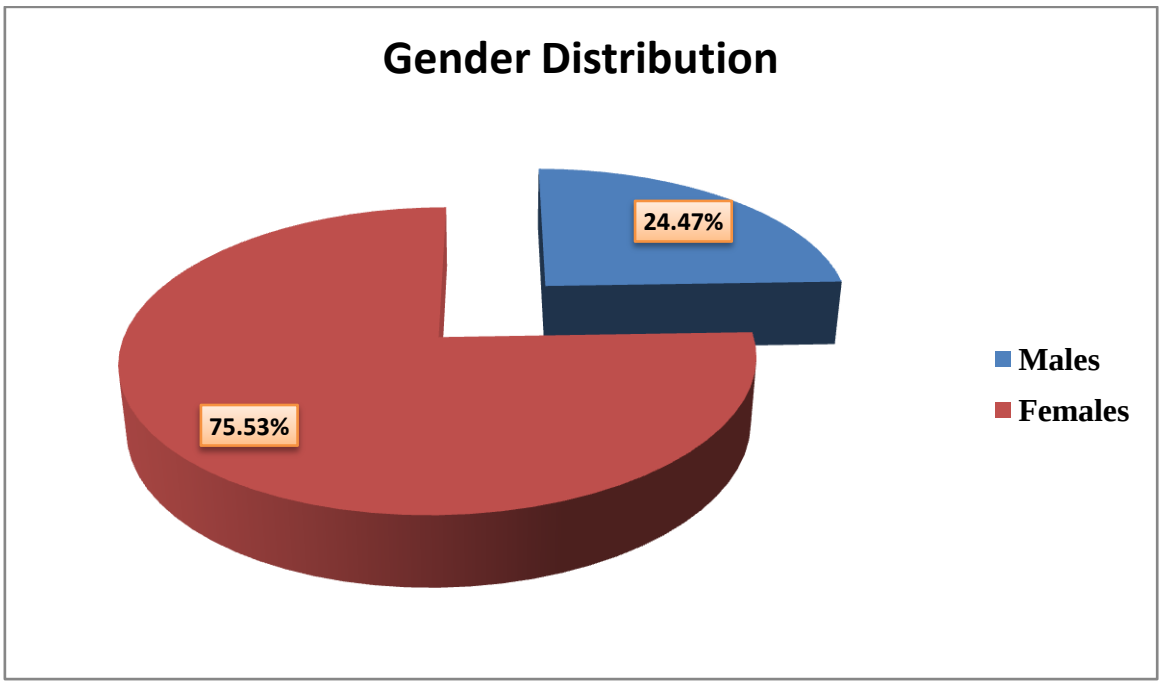
TABLE-2: Distribution of patients according to gender (N=143)

Gender	Number	Percent (%)
MALE	35	24.47
FEMALE	108	75.53
TOTAL	143	100.0

Comments:

Majority of the patients (75.53%) were females.

Chart 2: Percentage distribution the sample according to gender



ADEQUACY RATE :

Out of 143 FNACs, five aspirates were inadequate for cytological evaluation, hence they were labeled as unsatisfactory smears. They were categorized into category I of The Bethesda system.

The unsatisfactory smears had less than six clusters of follicular cells containing less than ten cells per cluster in a single smear.

The adequacy rate in our institution was 96% , the reason behind this high adequacy rate is we repeat FNAs in inadequate aspirates and if necessary FNAs are performed with ultrasound guidance.

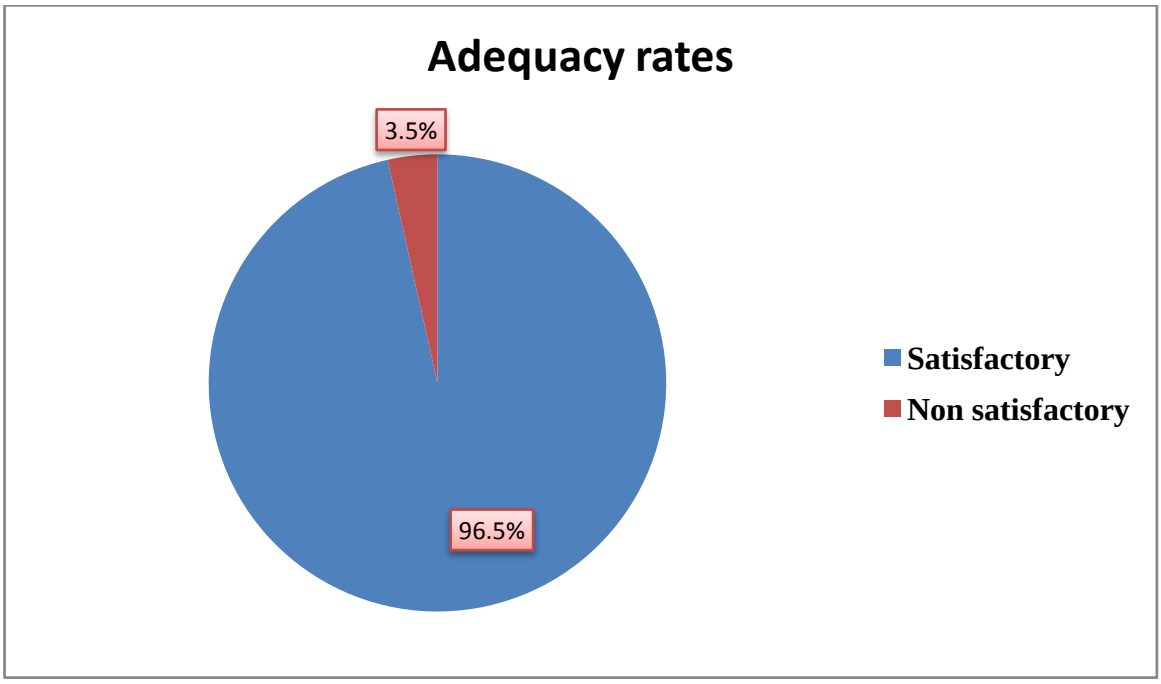
TABLE-3: Distribution of patients according to Adequacy rates in cytology (N=143)

Adequacy rates	Number	Percent (%)
Satisfactory	138	96.5
Non Satisfactory	5	3.5
TOTAL	143	100

Comments:

Majority of the patients (96.5%) presented with satisfactory adequacy rates in cytology.

Chart 3 : Percentage distribution of the sample according to adequacy rate



DISTRIBUTION OF LESIONS:

The Fine needle aspiration smears which were adequate for evaluation were categorized into non neoplastic and neoplastic lesions.

The non neoplastic lesions included colloid goitre, colloid goitre with cystic degeneration, hyperplastic nodule, and Hashimoto's thyroiditis. They come under category II of The Bethesda system. The non neoplastic lesions constituted the major proportion 86%.

The neoplastic lesions comprise of "Atypia of undetermined significance", "Follicular neoplasm or suspicious for follicular neoplasm and follicular neoplasm suspicious of Hurthle cell type", "suspicious of papillary carcinoma", and "malignancy".

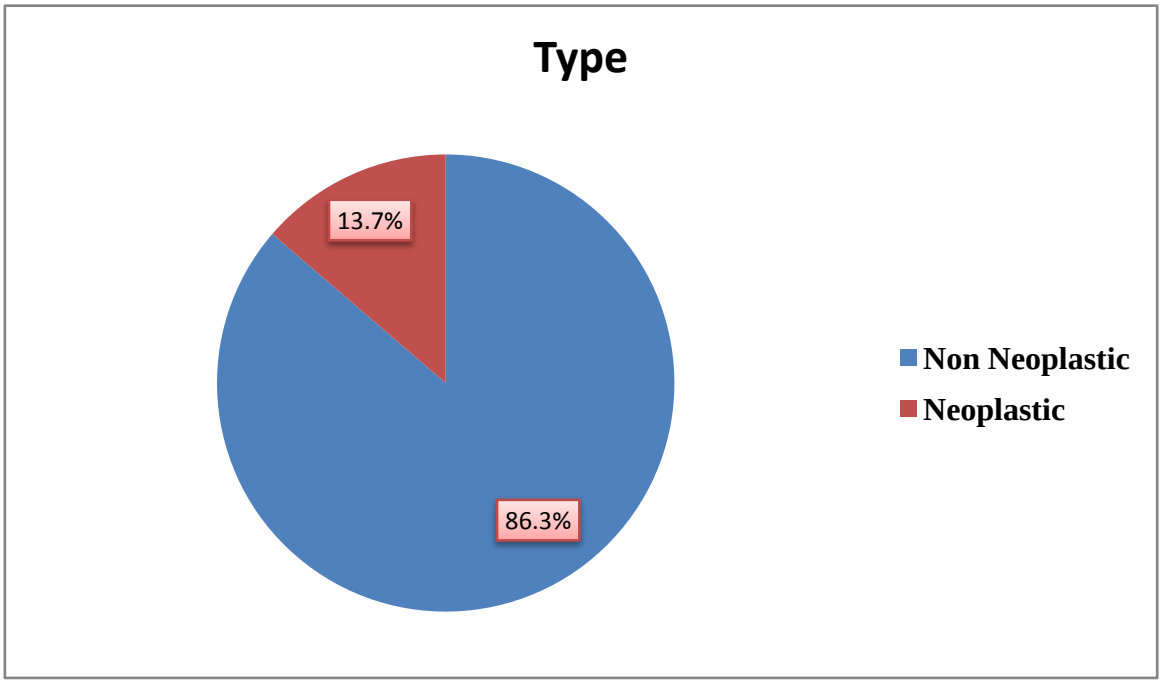
TABLE-4: Distribution of patients according to Neoplastic & Non neoplastic lesions (N=138)

Type	Number	Percent (%)
Neoplastic	19	13.7
Non Neoplastic	119	86.3
TOTAL	138	100

Comments:

Majority of the patients (86.3%) presented with Non Neoplastic lesions

Chart 4 : Percentage distribution of neoplastic and non neoplastic lesions



THE BETHESDA SYSTEM OF REPORTING THYROID CYTOPATHOLOGY : CATEGORIES

Among 143 cases, non neoplastic category II lesions were the major proportion constituting 83%, category I unsatisfactory smears were 5%, category III 0%, next highest percentage of cases were in category IV with 9%, category V and category VI had 2% of cases each.

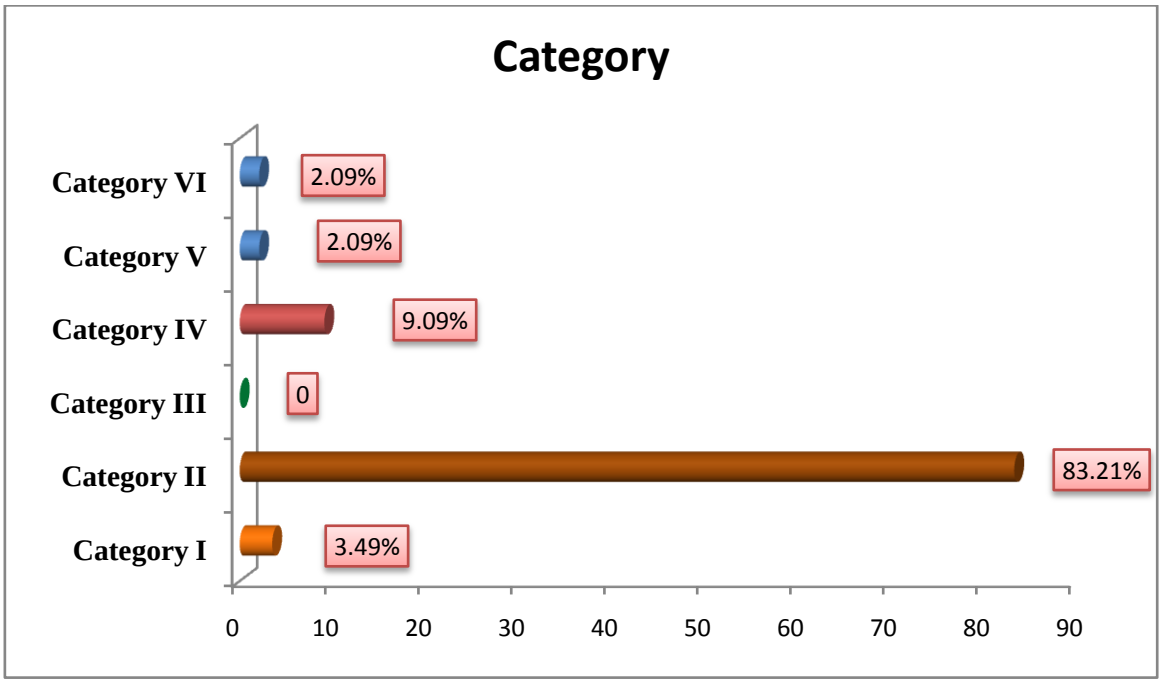
TABLE-5: Distribution of patients according to Bethesda system (N=143)

Categories	Number	Percent (%)
Category I	5	3.49
Category II	119	83.21
Category III	0	0
Category IV	13	9.09
Category V	3	2.09
Category VI	3	2.09
TOTAL	143	100

Comments:

Majority of the patients (83.21%) presented with Category II lesions.

Chart 5 : Percentage distribution of the sample according to Bethesda



<u>Category II</u> : Benign

The major proportion of cases were in the category II consisting of 119 cases. Among them colloid goitre was maximum with 70 cases, next was colloid goitre with cystic degeneration 40 cases, hyperplastic nodule 5 cases and 4 cases of hashimoto's thyroiditis seen in present study.

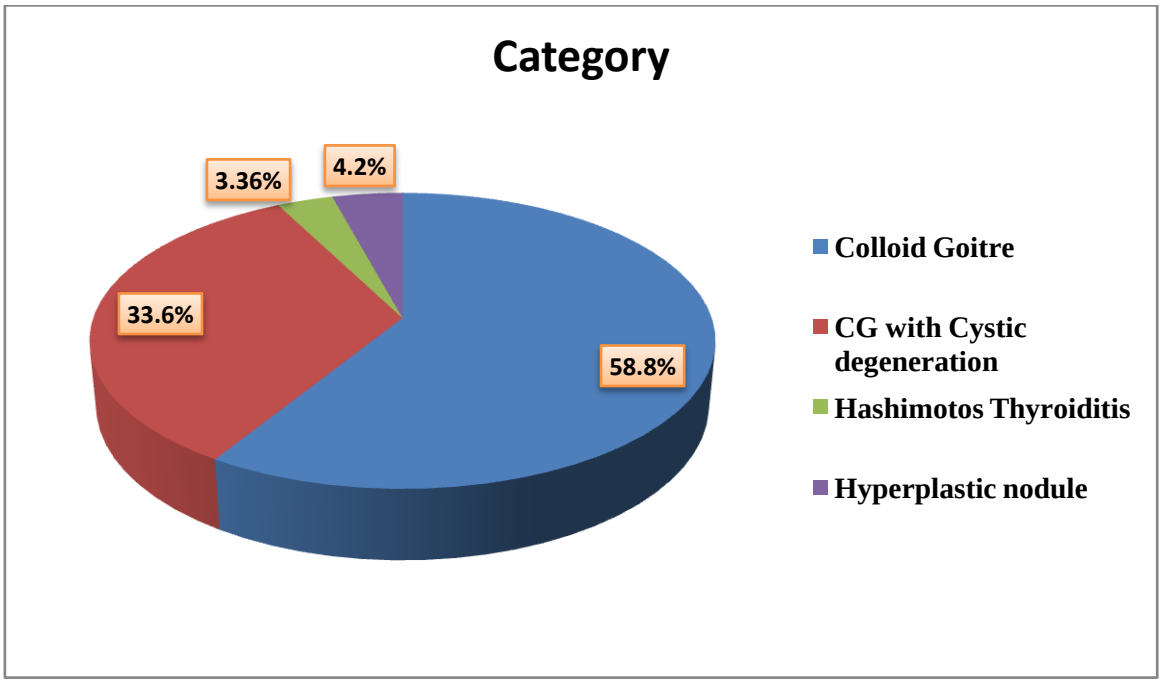
TABLE-6: Distribution of patients according to Category II (N=119)

Categories	Number	Percent (%)
Colloid goitre	70	58.8
Colloid goitre with cystic degeneration	40	33.6
Hashimotos' Thyroiditis	4	3.36
Hyperplastic nodule	5	4.20
TOTAL	119	100

Comments:

Majority of the patients (58.8%) presented with Colloid goiter.

Chart 6 : Percentage distribution in benign category



Colloid goitre/ colloid goitre with degeneration

Among Colloid goitre patients, majority of them belonged to the age group of 31-40 years and 41- 50 years.

Microscopic features :

Smears showed scant to moderate cellularity. Smears had follicular cells arranged in microfollicles and monolayered sheets . Follicular cells had regular round nuclei with fragile gray blue cytoplasm. Occasionally many bare nuclei and Hurthle cells were seen. Background showed abundant colloid which appeared green to pink with Papanicolaou stain and blue violet with MGG stain. Colloid showed pavement like appearance.(Figure 1)

Cases with fluid aspirate from cysts showing cyst macrophages and hemosiderin laden macrophages were reported as colloid goitre with cystic degeneration.(Figure 2)

In present study, colloid goitre and colloid goitre with cystic degeneration accounted for 110 cases out of 143 cases.

Hyperplastic nodule:

Smears studied were moderately cellular . Follicular cells were arranged in microfollicles, macrofollicles and monolayered sheets. Background showed scant to absent colloid.

Out of 115 cases of colloid goitre (including cystic degeneration and hyperplastic nodule) 96.5% cases were positively correlated. Histologically remaining turned out to be Papillary carcinoma in 3 cases and Papillary microcarcinoma in one case. These discordant cases were 2 cases each of colloid goitre and colloid goitre with degeneration in cytology. Among 5 cases of hyperplastic nodule 4 was adenomatous goitre and one was follicular adenoma in histopathology.

Hashimoto's thyroiditis

Four cases of hashimoto's thyroiditis was diagnosed in cytology in our study. All the four cases were female and were in third decade.

Microscopic features :

Smears showed moderate cellularity. Follicular cells were arranged in microfollicles and monolayered sheets. Many lymphoid cells were seen impinging on the follicular cells. Polymorphic population of lymphoid cells were seen in the background including plasma cells. Hurthle cells were seen singly scattered or arranged in clusters. Hurthe cells have distinct cell border, abundant finely granular cytoplasm and large nuclei . Some hurthle cells showed nuclear atypia and prominent nucleoli.(Figure3)

Out of four cases of Hashimoto's thyroiditis diagnosed in cytopathology, 3 cases were Hashimoto's thyroiditis in histopathology. One case turned out to be multinodular goitre.

NEOPLASTIC LESIONS OF THE THYROID GLAND :

Neoplastic lesions of thyroid according to the Bethesda system comprises of lesions from category III to category VI.

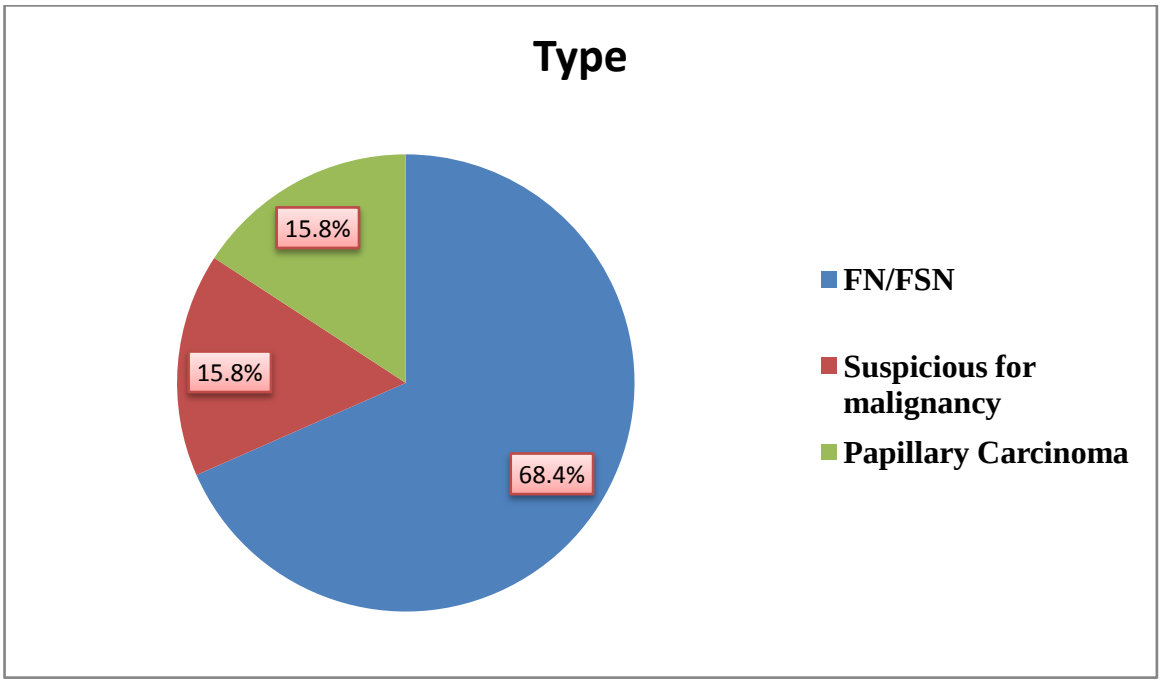
TABLE-7: Distribution of patients according to Neoplastic lesions (N=19)

Type	Number	Percent (%)
Atypia of undetermined significance (Category III)	0	0
FN/SFN (Category IV)	13	68.4
Suspicious for malignancy (Category V)	3	15.8
Papillary Carcinoma (Category VI)	3	15.8
TOTAL	19	100

Comments:

Majority of the Neoplastic lesions (68.4%) were of Category IV (FN/SFN)

Chart 7 : Percentage distribution of neoplastic lesions



Category III : Atypia of undetermined significance

In present study no cases were diagnosed in this category

Category IV : "Follicular neoplasm/ Hurthle cell neoplasm, suspicious for follicular neoplasm/ Hurthle cell neoplasm":

There were thirteen cases in this category. The patients of this category had a wide range of age, from 20 years to 70 years. Eight patients were females and remaining five were males.

Microscopy features :

Smears had moderate to marked cellularity. Smears had many uniform sized microfollicle clusters in a background of scant colloid. Follicular cells had large round nuclei with inconspicuous nucleoli and scant amount of cytoplasm. Nuclear overlapping and synctial aggregates were occasionally seen.

Out of the thirteen cases 7 cases had non neoplastic diagnosis in histopathology which includes 4 cases adenomatous goitre, 2 cases of Hashimoto's thyroiditis and 1 case of nodular goitre.

Remaining six cases comprised of 1 case of Follicular carcinoma, 1 case of primary lymphoma of thyroid- marginal zone type, and 4 cases of Papillary carcinoma. One case of Papillary carcinoma was follicular variant.

In Papillary carcinoma category three patients were in the second decade. Two were females and one was male. Other patient with Follicular variant of papillary carcinoma was 44 years old male. Both Follicular carcinoma and Lymphoma thyroid patients were in the sixth decade.

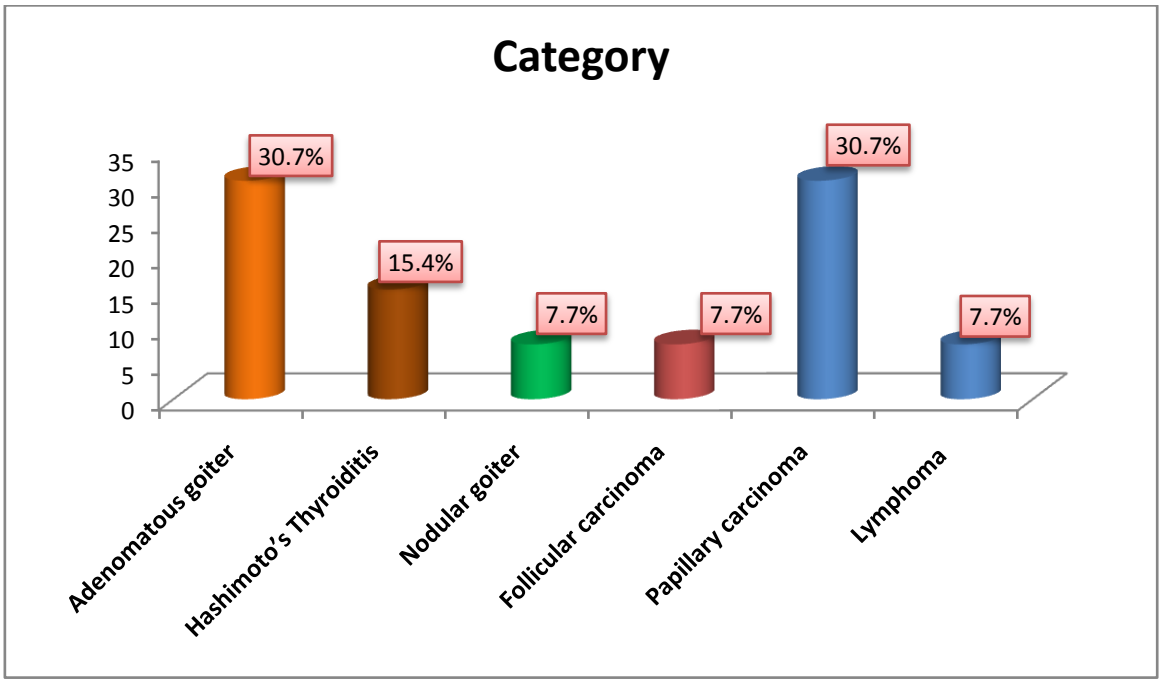
TABLE-8: Distribution of FN/SFN (Category IV) in Histopathology (N=13)

Categories	Number	Percent (%)
Adenomatous goiter	4	30.7
Hashimoto's Thyroiditis	2	15.4
Nodular goiter	1	7.7
Follicular carcinoma	1	7.7
Papillary carcinoma and its follicular variant	4	30.7
Lymphoma	1	7.7
TOTAL	13	100

Comments:

Majority of FN/SFN (Category IV) in Histopathology were both adenomatous goitre and papillary carcinoma each constituting 30.7% of cases.

Chart 8 : Distribution of histopathology of Follicular neoplasm(FN) / SFN



Category V: Suspicious for malignancy

In present study there were three cases in this category. One case each of Multinodular goitre, Follicular variant of papillary carcinoma and Follicular carcinoma.

Follicular variant of papillary carcinoma patient was a 29 year old female. Follicular carcinoma patient was 57 year old male.

Microscopic features :

Smears had moderate to high cellularity. Follicular cells were arranged in macrofollicles predominantly, admixed among the benign looking follicular cells with some follicular cells having nuclear enlargement and mild nuclear pallor. Occasionally nuclear grooves, irregular nuclear membrane and nuclear molding and overlapping were seen.

TABLE-9: Distribution of Suspicious for malignancy (Category V) in Histopathology (N=3)

Categories	Number	Percent (%)
Multinodular goiter	1	33.3
Follicular variant of Papillary carcinoma	1	33.3
Follicular carcinoma	1	33.3
TOTAL	3	100

Comments:

Of the 3 cases of Suspicious for malignancy (Category V) in histopathology, one is Multinodular goiter (33.3%), second is Follicular variant of Papillary carcinoma (33.3%) and other is Follicular carcinoma (33.3%).

Category VI : Malignant

Cytologically 3 cases were diagnosed as Papillary carcinoma in present study. All the three cases were Papillary carcinoma in histopathology. There was 100% correlation in category VI. One patient was 16 years old female and other two were males in the sixth decade.

Microscopic features :

Smears studied were highly cellular. They showed many papillae with or without fibrovascular cores formed by follicular cells. Papillae had anatomical bordering. Follicular cells had large nuclei with irregular nuclear membrane, powdery chromatin. Nuclear overlapping and crowding were noted. Some nuclei showed intranuclear cytoplasmic inclusions and longitudinal grooves. (Figure 4- 10)

TABLE-10: Distribution of Category VI in Histopathology (N=3)

Categories	Number	Percent (%)
Papillary carcinoma	3	100
TOTAL	3	100

Comments:

All the 3 cases of (Category VI) in histopathology are Papillary carcinoma (100%).

HISTOPATHOLOGY DISTRIBUTION

There were 72 cases of colloid goitre(Figure 11, Fig 13), 4 cases of colloid goitre with degeneration(Figure 12), 23 cases of Adenomatous goitre, 17 cases of Hashimoto's thyroiditis(Fig 14), 12 cases of Follicular adenoma(Fig 15), 2 cases of Follicular carcinoma(Fig 22,23), 12 cases of Papillary carcinoma(Fig 16-21) including 2 cases of Follicular variant of papillary carcinoma and one case of primary marginal zone lymphoma of thyroid (Fig 24).

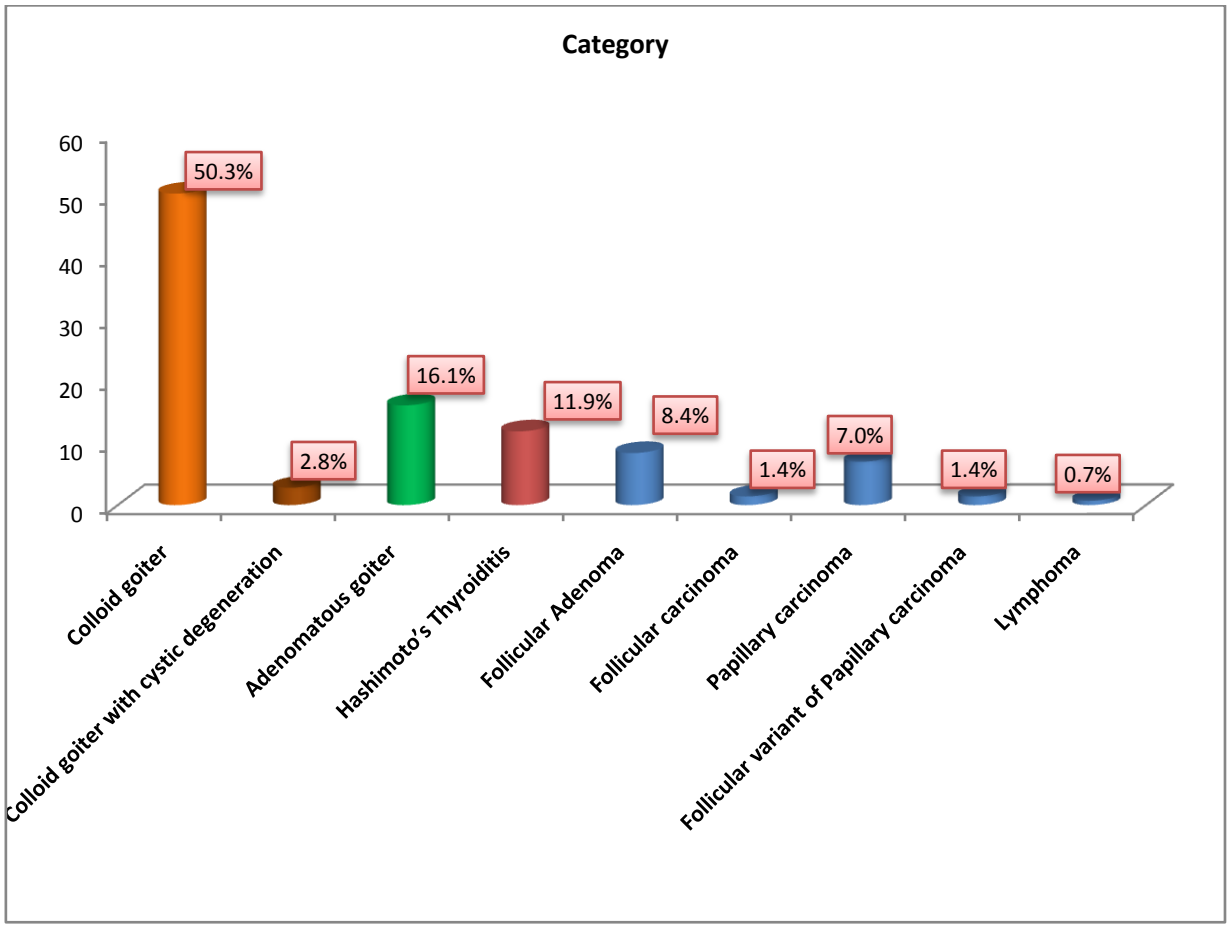
TABLE-11: Distribution of patients according to diagnosis in Histopathology (N=143)

Categories	Number	Percent (%)
Colloid goiter	72	50.3
Colloid goiter with cystic degeneration	4	2.8
Adenomatous goiter	23	16.1
Hashimoto's Thyroiditis	17	11.9
Follicular Adenoma	12	8.4
Follicular carcinoma	2	1.4
Papillary carcinoma	10	7.0
Follicular variant of Papillary carcinoma	2	1.4
Lymphoma	1	0.7
TOTAL	143	100

Comments:

Majority of patients in histopathology (50.3%) presented with Colloid Goitre.

Chart 9 : Percentage distribution of the sample according to histopathology



Malignancy rate of each Bethesda category:

From the histopathological data malignancy rate of each category of the Bethesda system was calculated. In present study malignancy rate of category II was 3.4%, 46% for category IV, 66% for category V and 100% for category VI lesions.

Table-12: Malignancy rate of each Bethesda category

Bethesda category	Malignancy rate (%)
I	0
II	3.4
III	0
IV	46
V	66
VI	100

STATISTICAL ANALYSIS:

True positive, true negative, false positive and false negative results were obtained. From those values sensitivity, specificity, positive predictive value, negative predictive value were calculated.

TABLE-13: 2 x 2 Contingency table comparing Bethesda system with Histopathology (N=138)

Bethesda system	Histopathology		TOTAL
	Carcinoma	Benign	
Carcinoma	3 (TP)	0 (FP)	3
Benign	12 (FN)	123 (TN)	135
TOTAL	15	123	138

	Indicators	Percentage
1.	**Sensitivity = TP/(TP+FN)**	**20%**
2.	**Specificity = TN/(TN+FP)**	**100%**
3.	**Positive Predictive Value = TP/(TP+FP)**	**100%**
4.	**Negative Predictive Value = TN/(TN+FN)**	**91.1%**

Colour Plates

MICROSCOPY

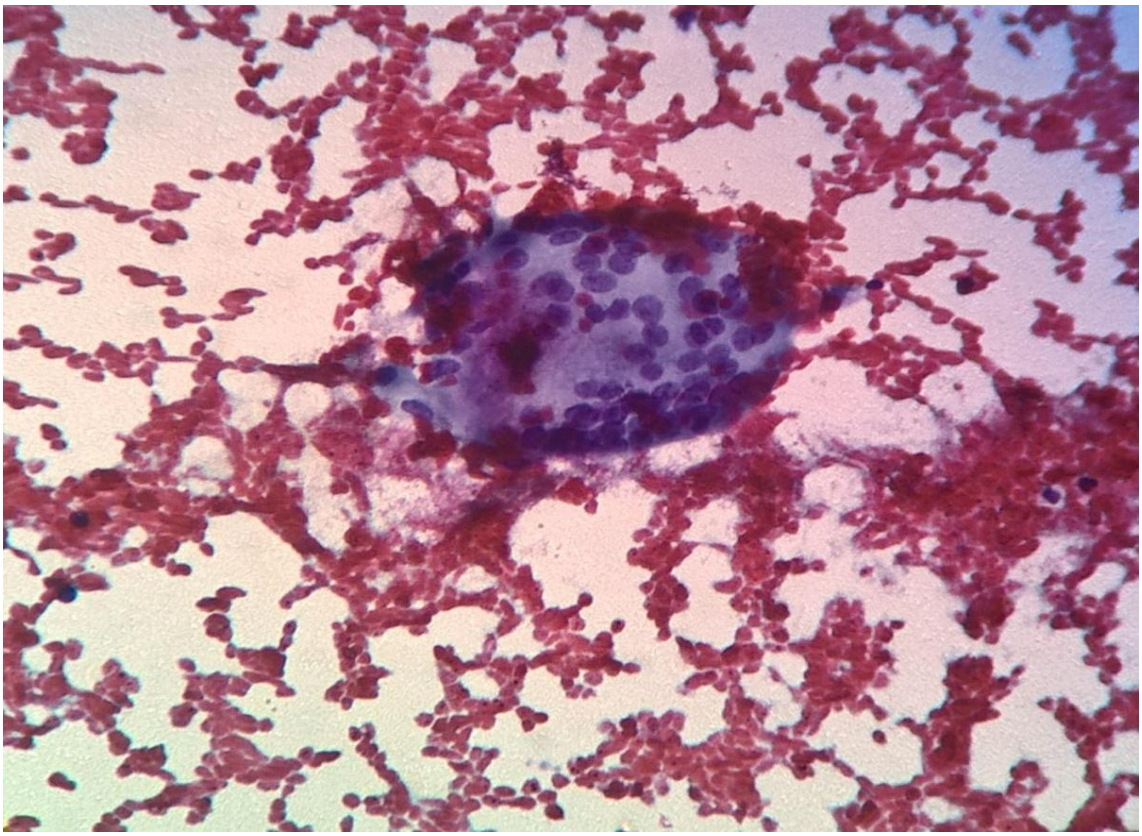


Figure 1 : Follicle in colloid goitre (10 X) Pap stain

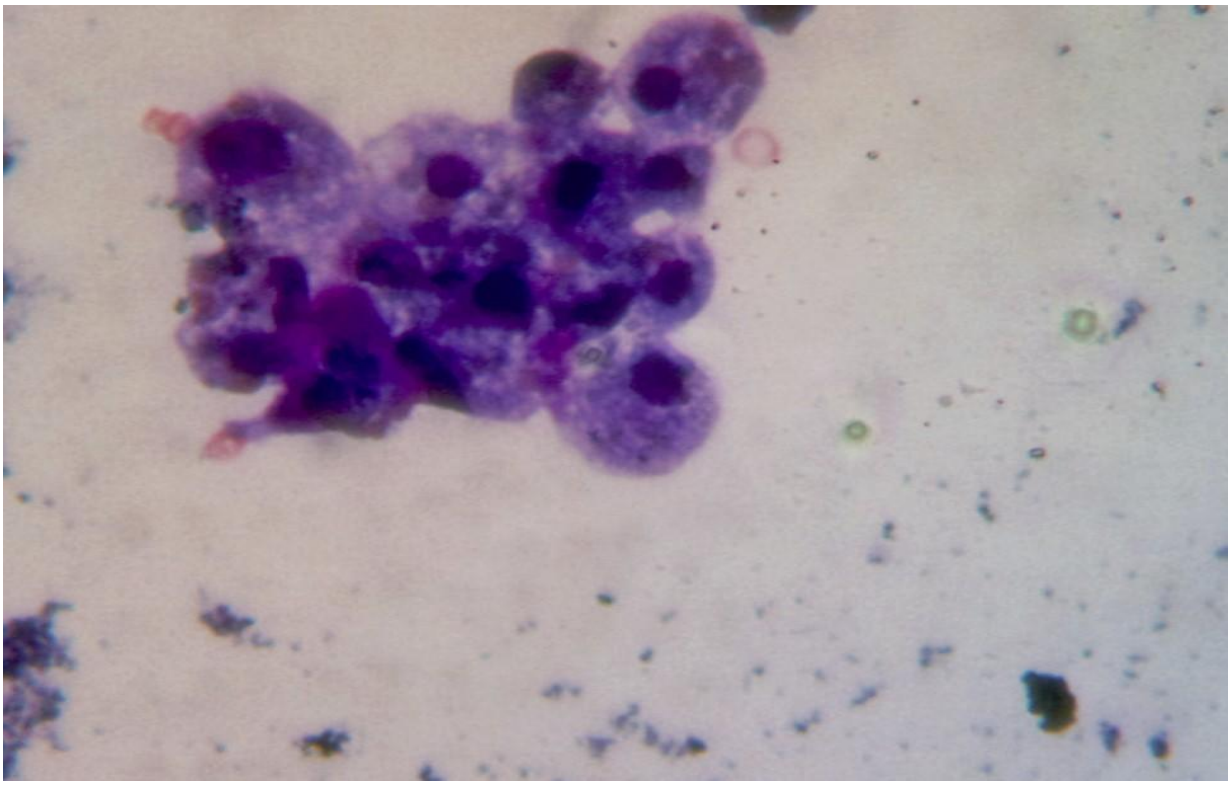


Figure 2 : Cyst macrophages in colloid goiter with cystic degeneration (40X) MGG stain

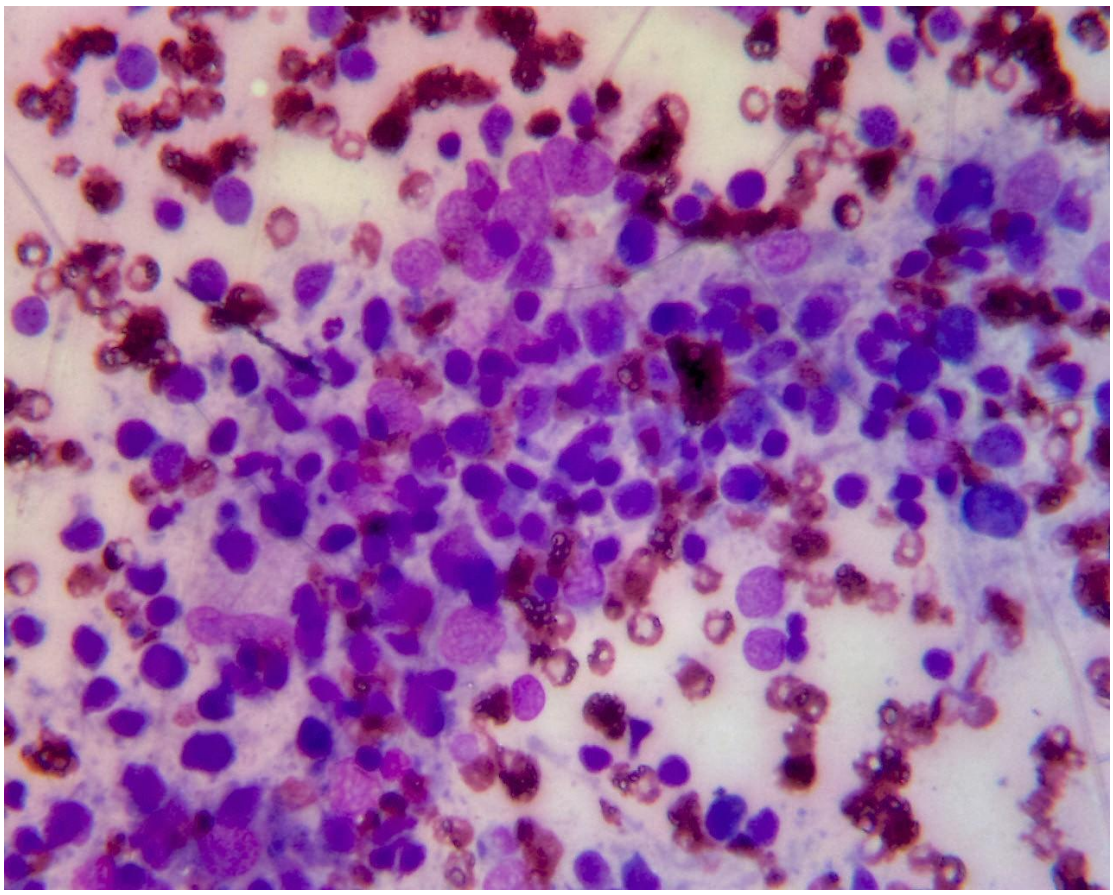


Figure 3 : Lymphocytes impinging on follicular cells in Hashimoto's thyroiditis (40 X) MGG stain

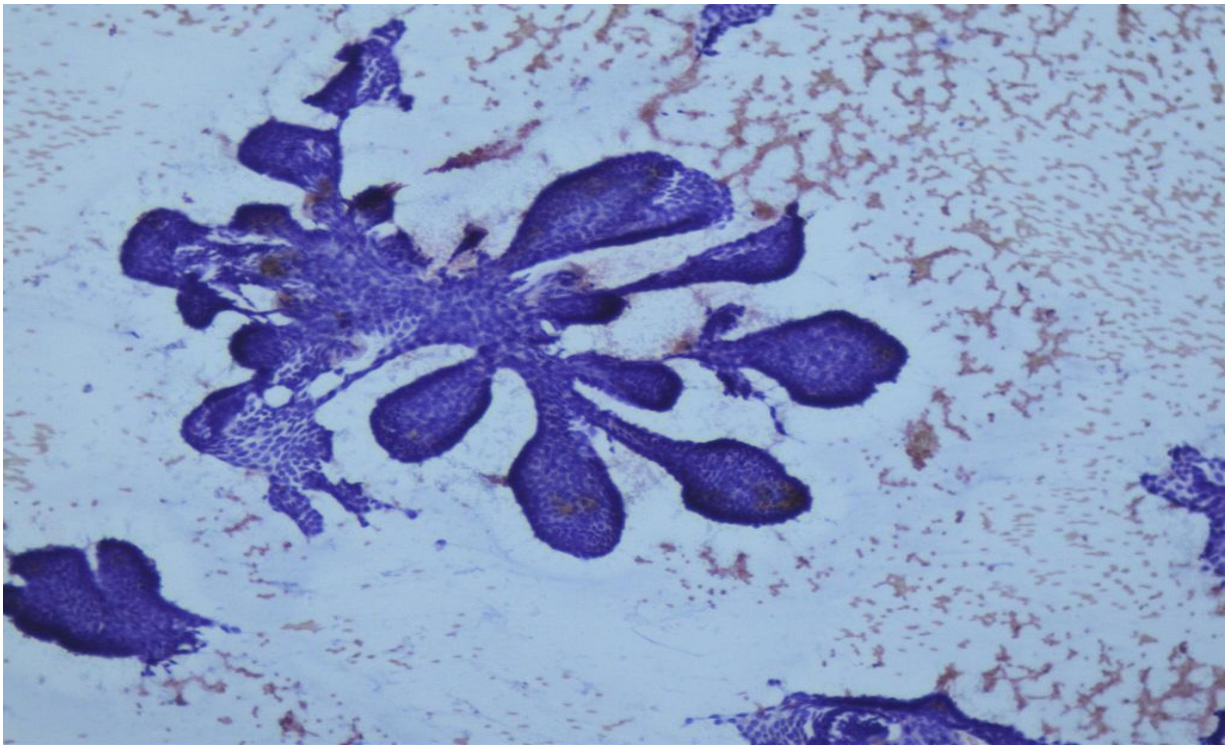


Figure 4: Papillaroid clusters in Papillary carcinoma thyroid (40X) Pap stain

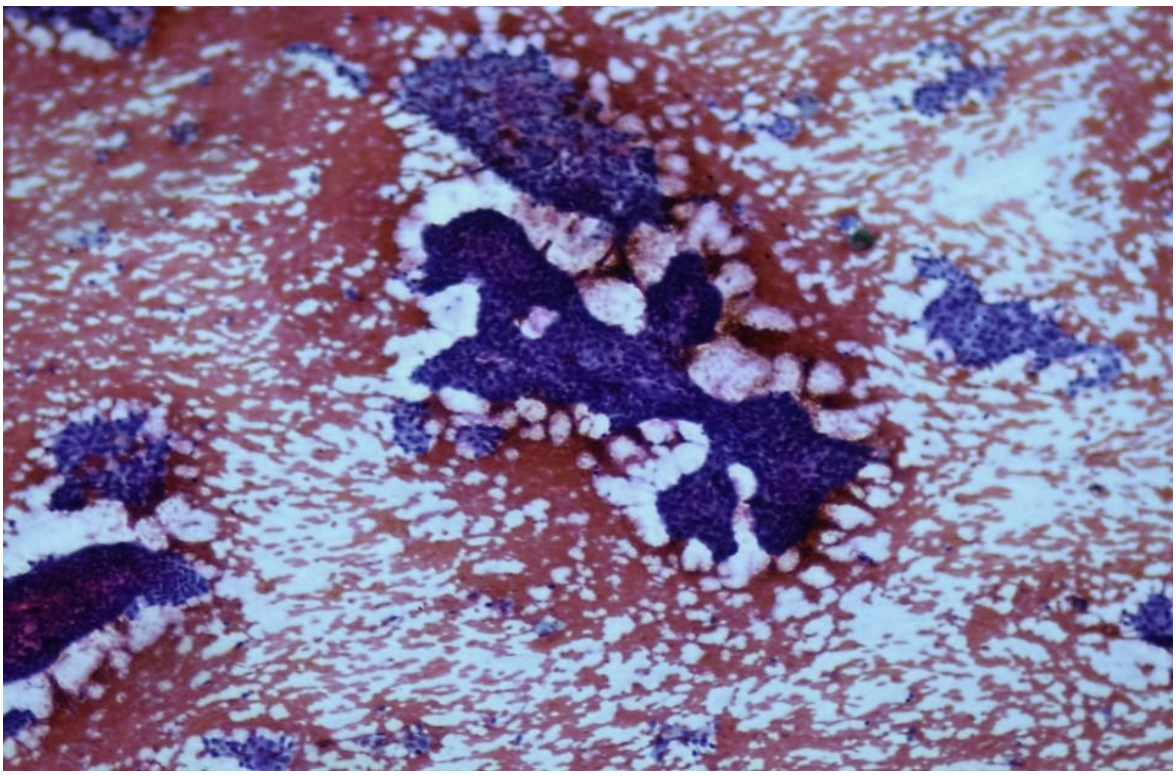


Figure 5 : Papillae in Papillary carcinoma thyroid (40X) Pap stain

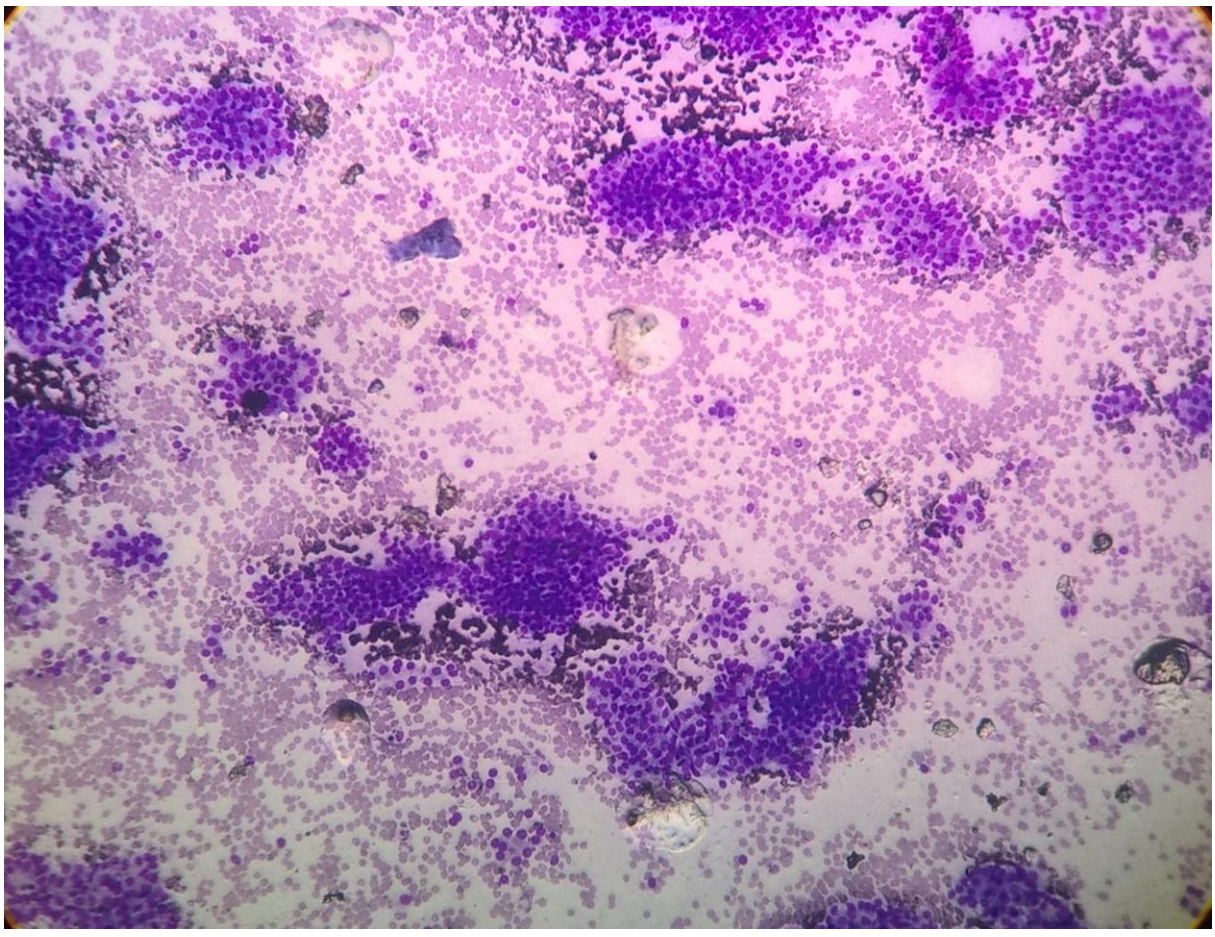


Figure 6: Increased cellularity in Papillary carcinoma thyroid (10X) MGG stain

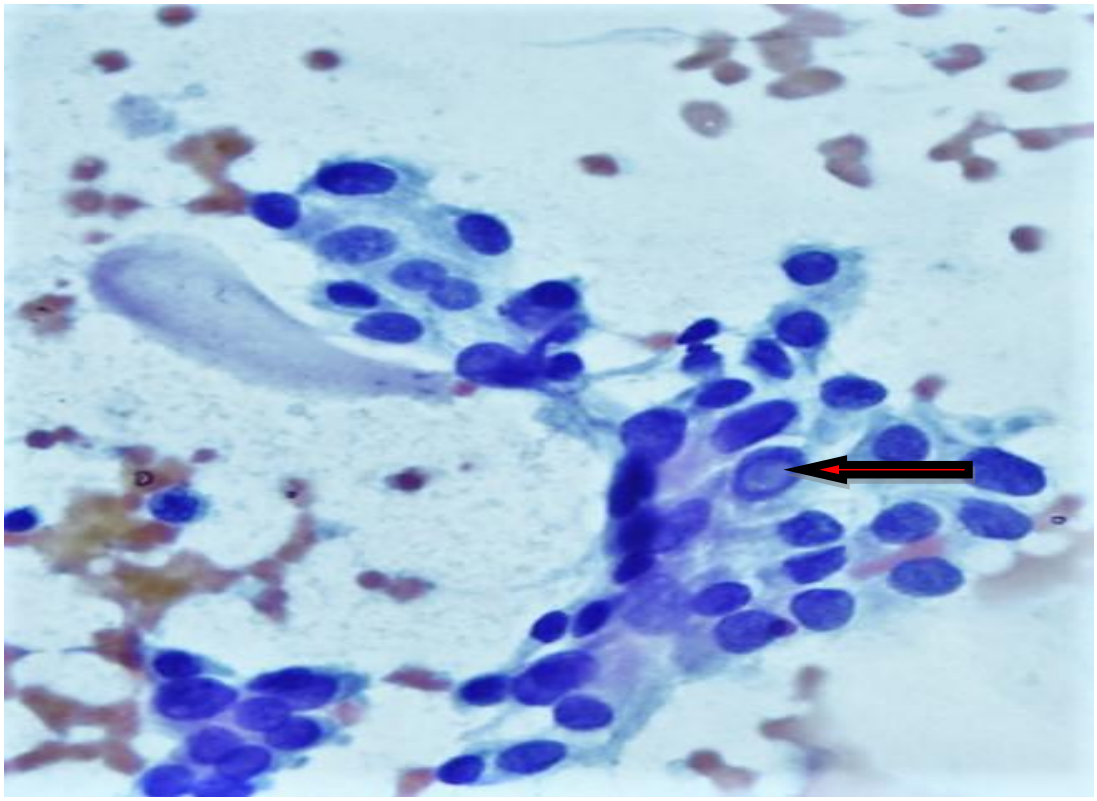


Figure 7 : Intranuclear inclusions in Papillary carcinoma thyroid(100X), Pap stain

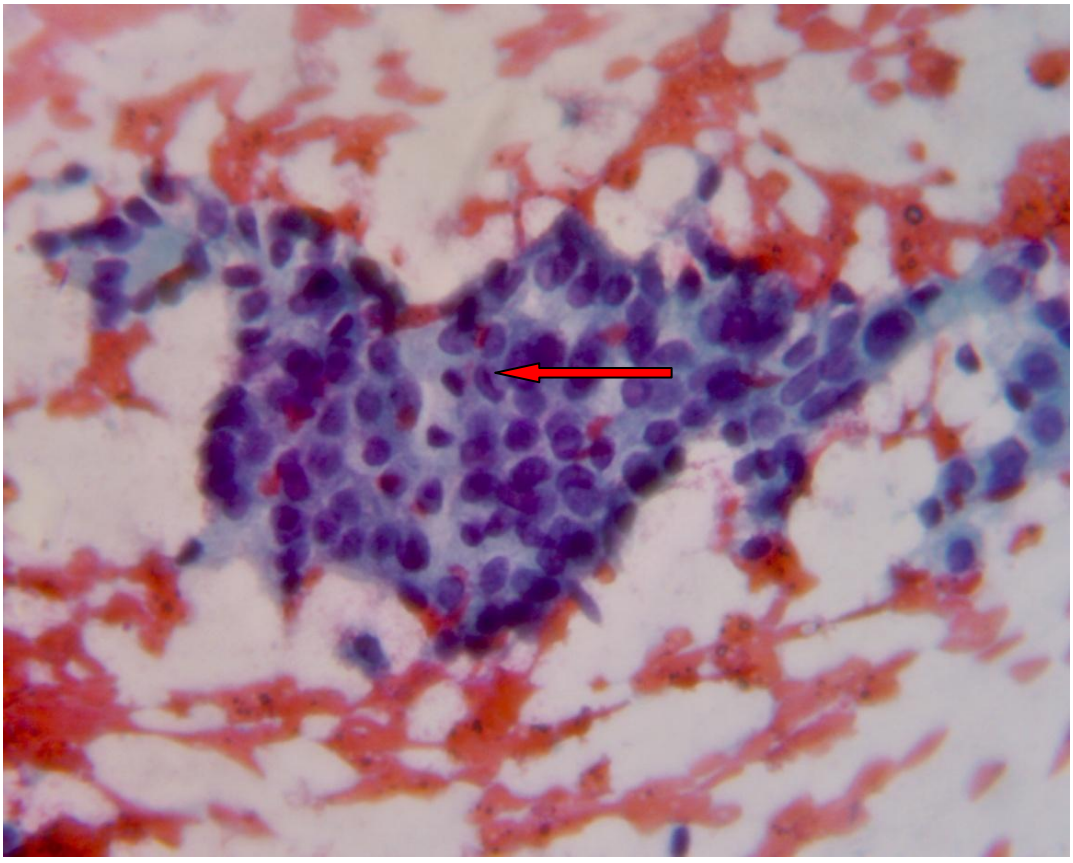


Figure 8: Nuclear groove in Papillary carcinoma thyroid (40X) Pap stain

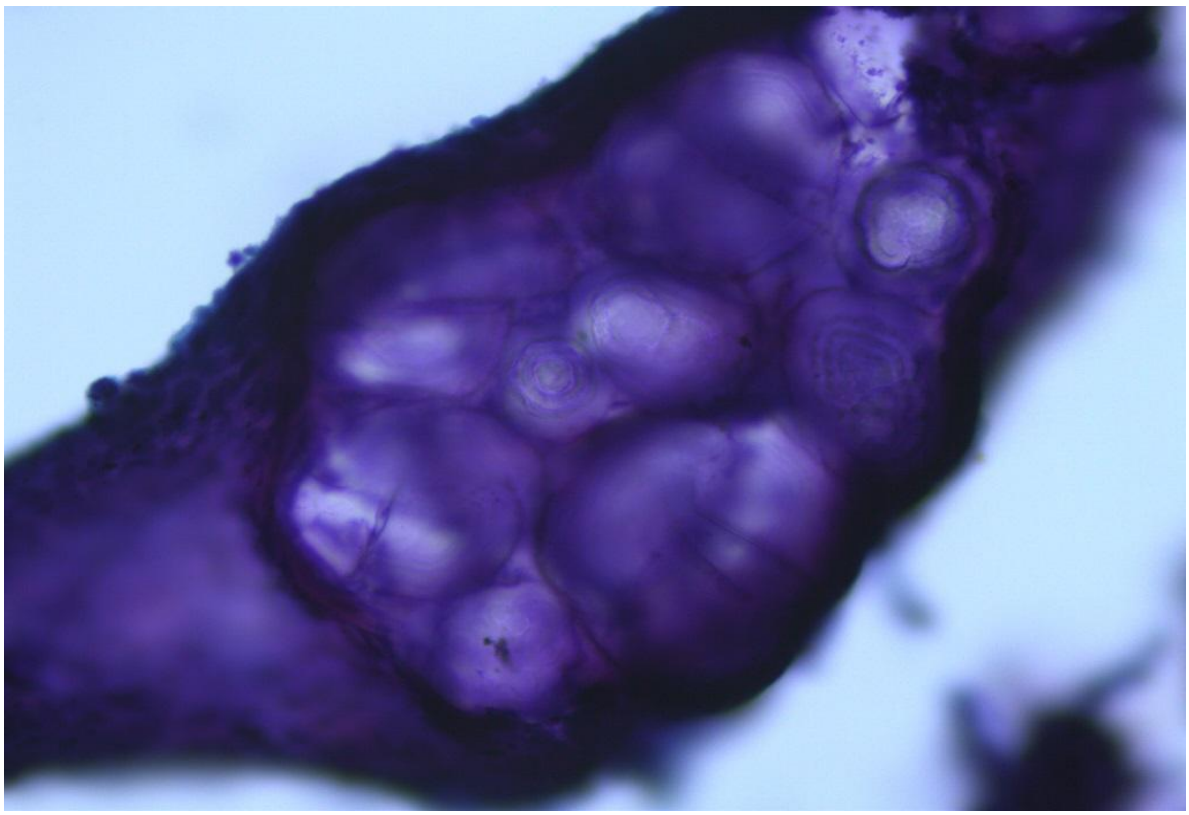


Figure 9 : Psammoma body in Papillary carcinoma thyroid (100X) Pap stain

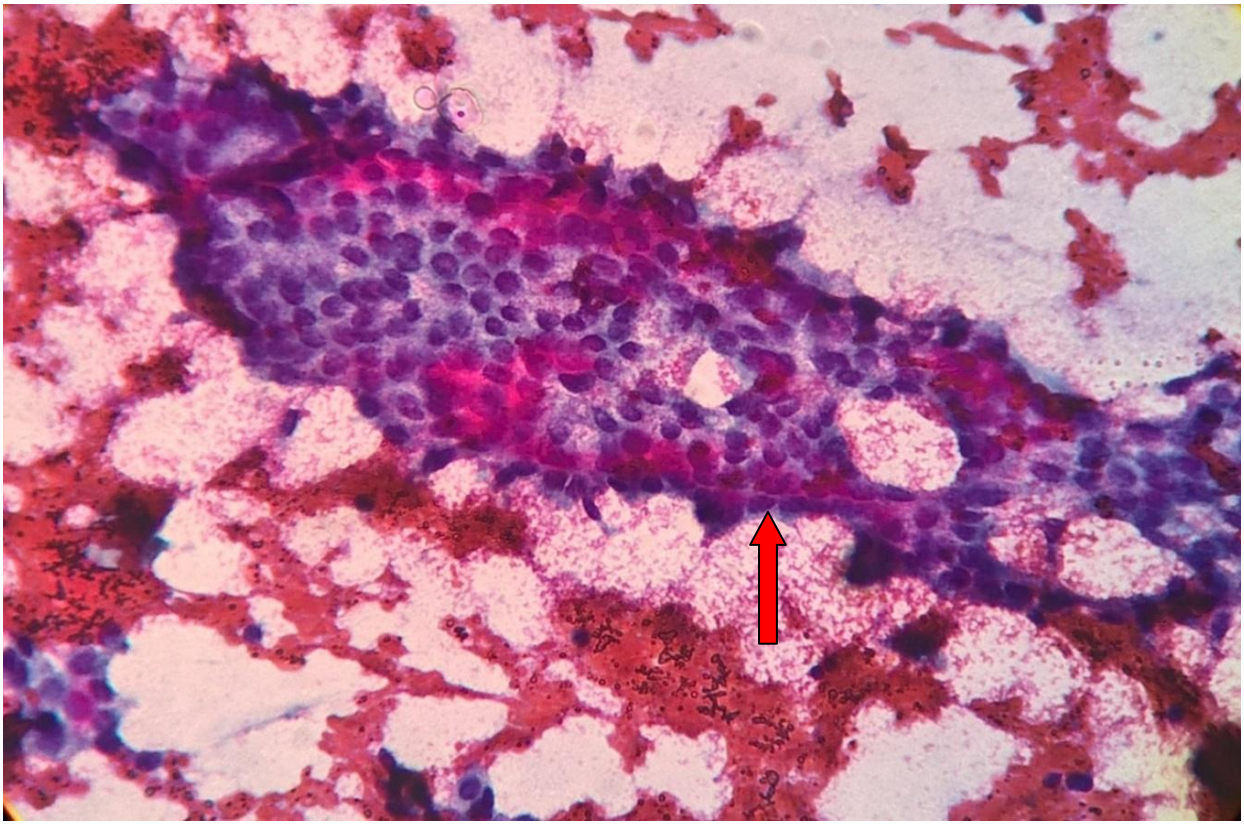


Figure 10: Anatomical border in Papillary carcinoma thyroid (40X) Pap stain

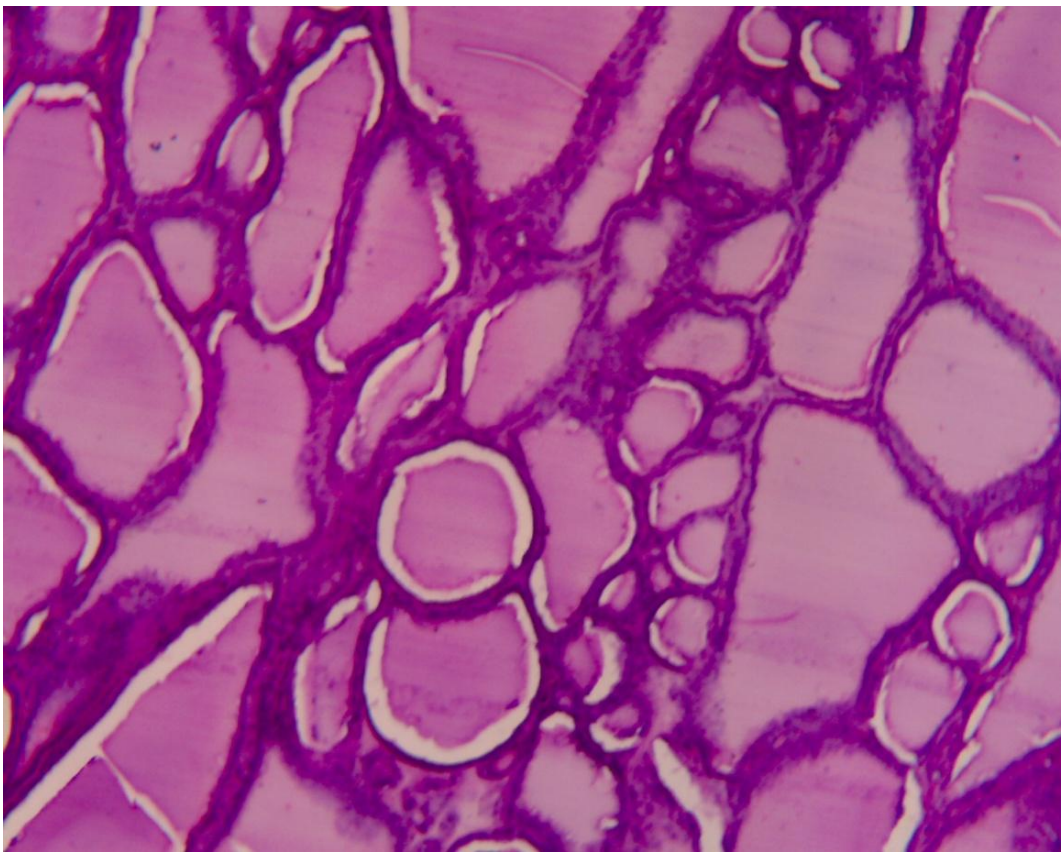


Figure 11 : Multinodular goitre (40X), H& E stain

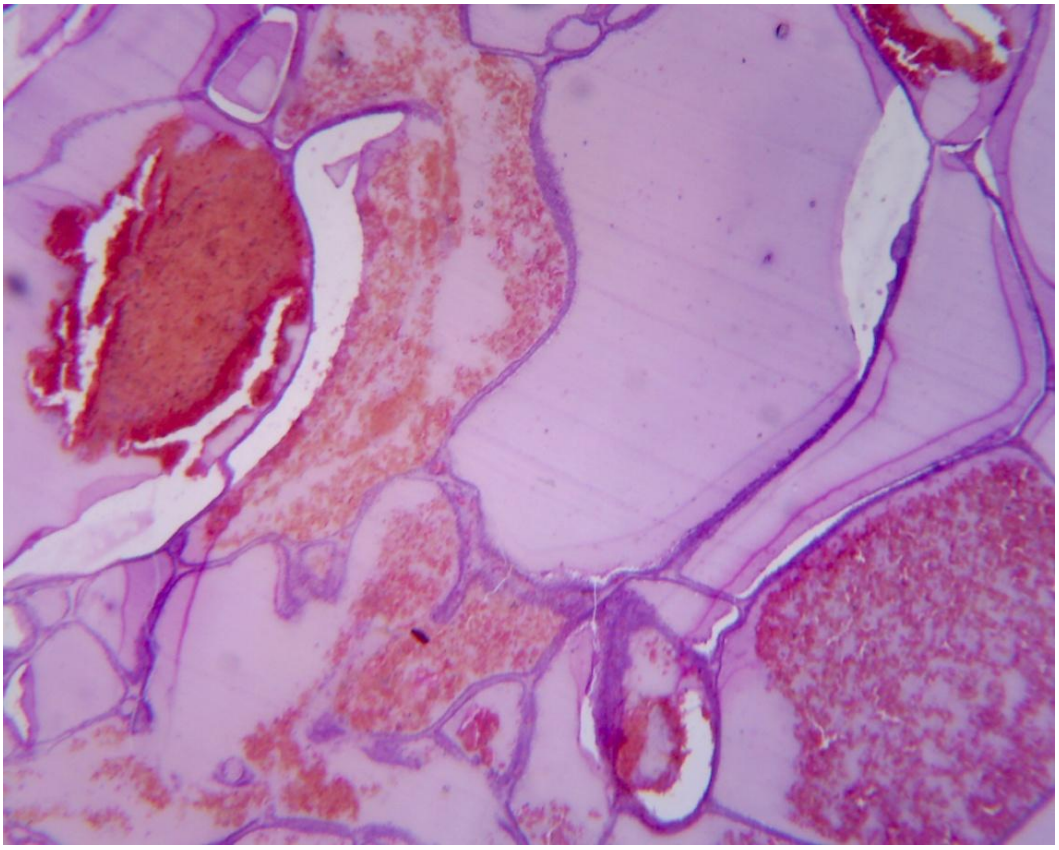


Figure 12: Colloid goitre with cystic degeneration and hemorrhage (40X) H&E stain

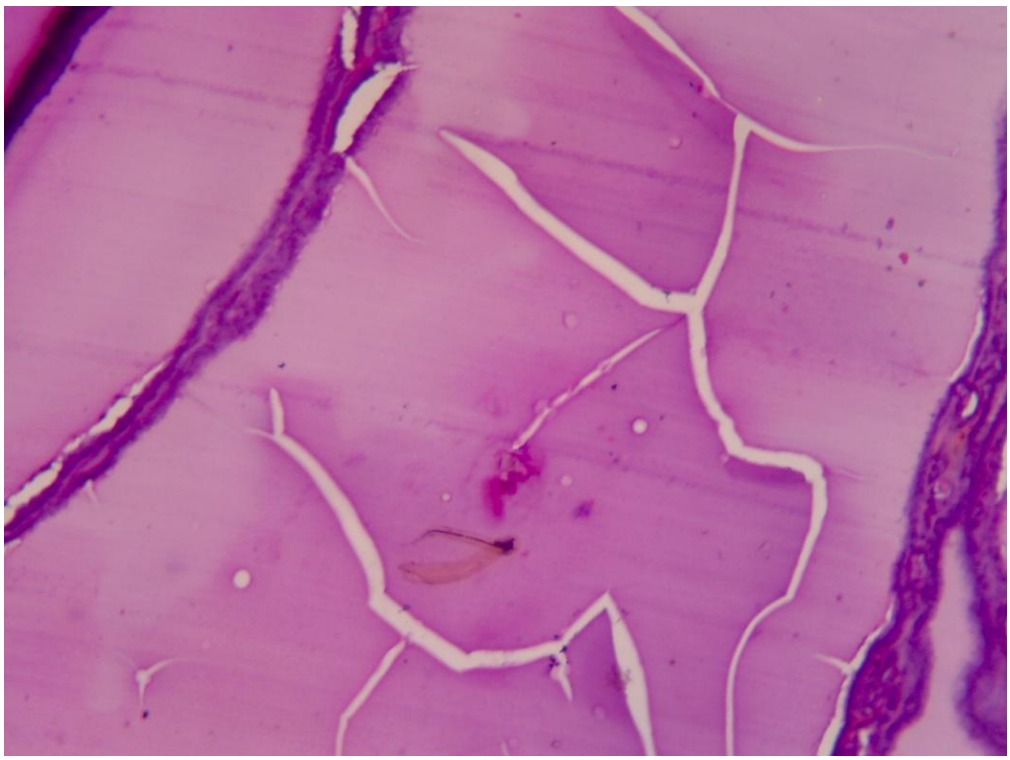


Figure 13: Retraction artifact of colloid in nodular colloid goitre (40X) H&E stain

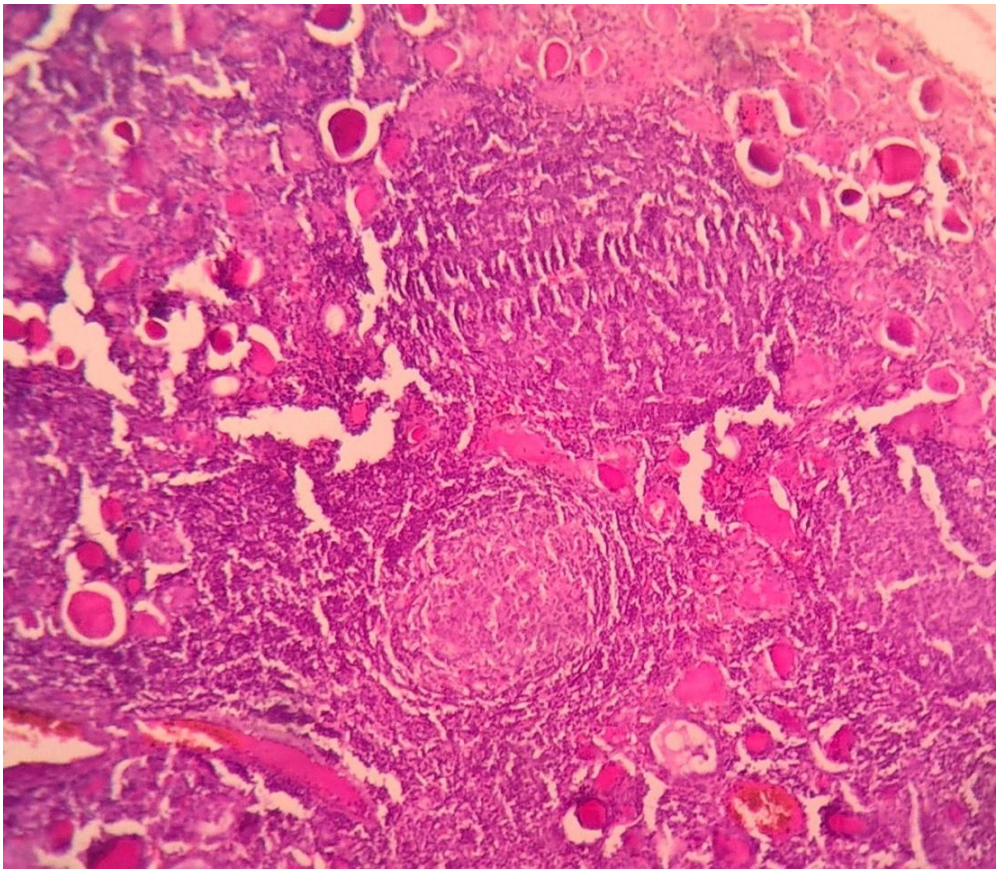


Figure 14: Lymphoid follicles with germinal centre in Hashimoto's thyroiditis (40X) H&E stain

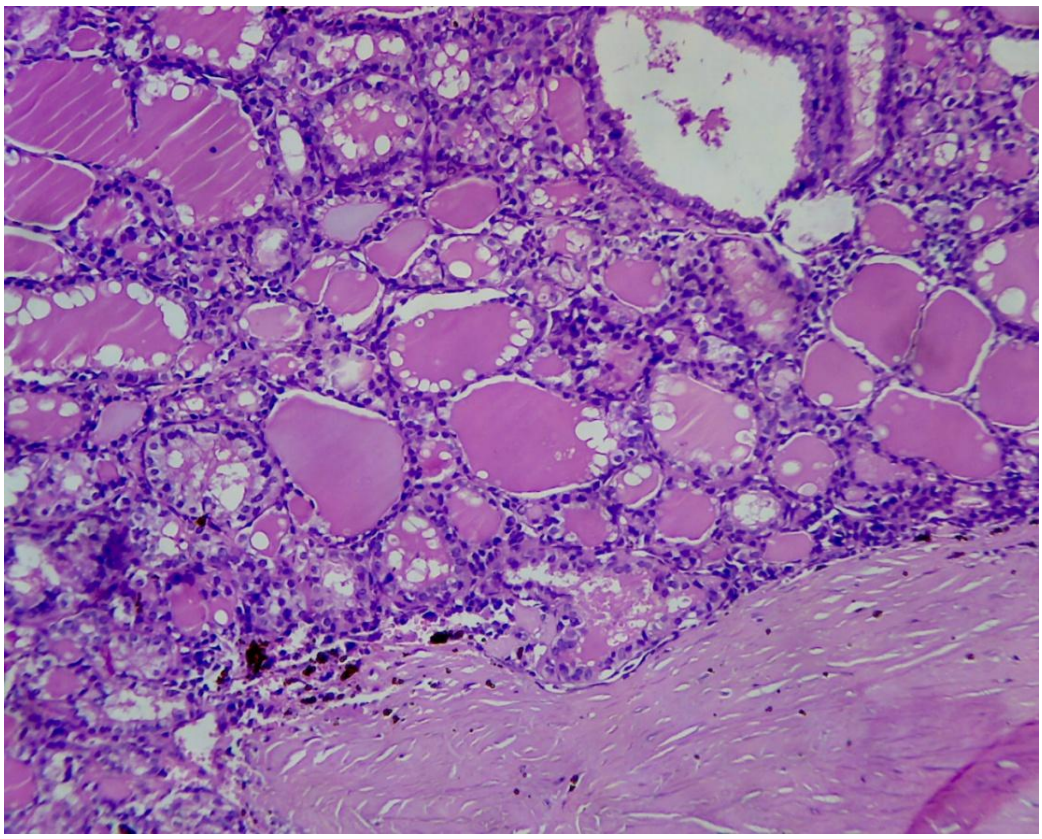


Figure 15 : Closely packed follicles in Follicular adenoma(40X) H&E stain

Figure 16 : Gross picture of Papillary carcinoma thyroid

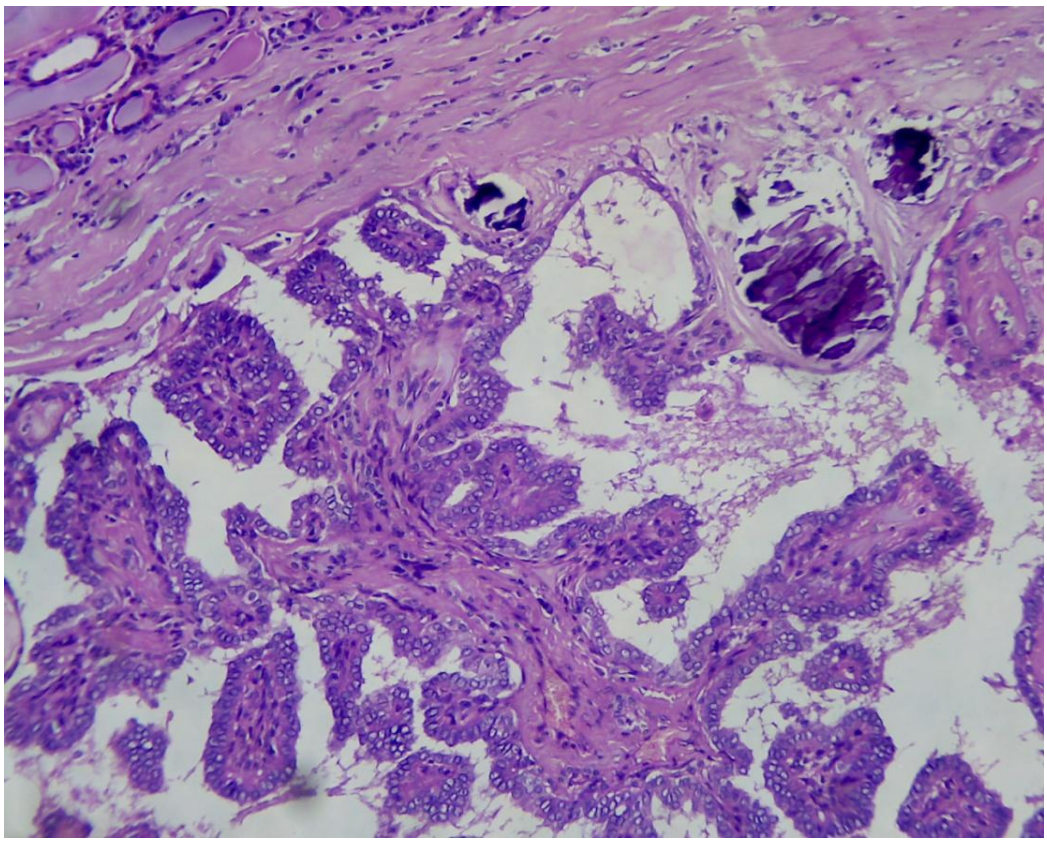


Figure 17: Papillae in Papillary carcinoma thyroid (10X), H&E stain

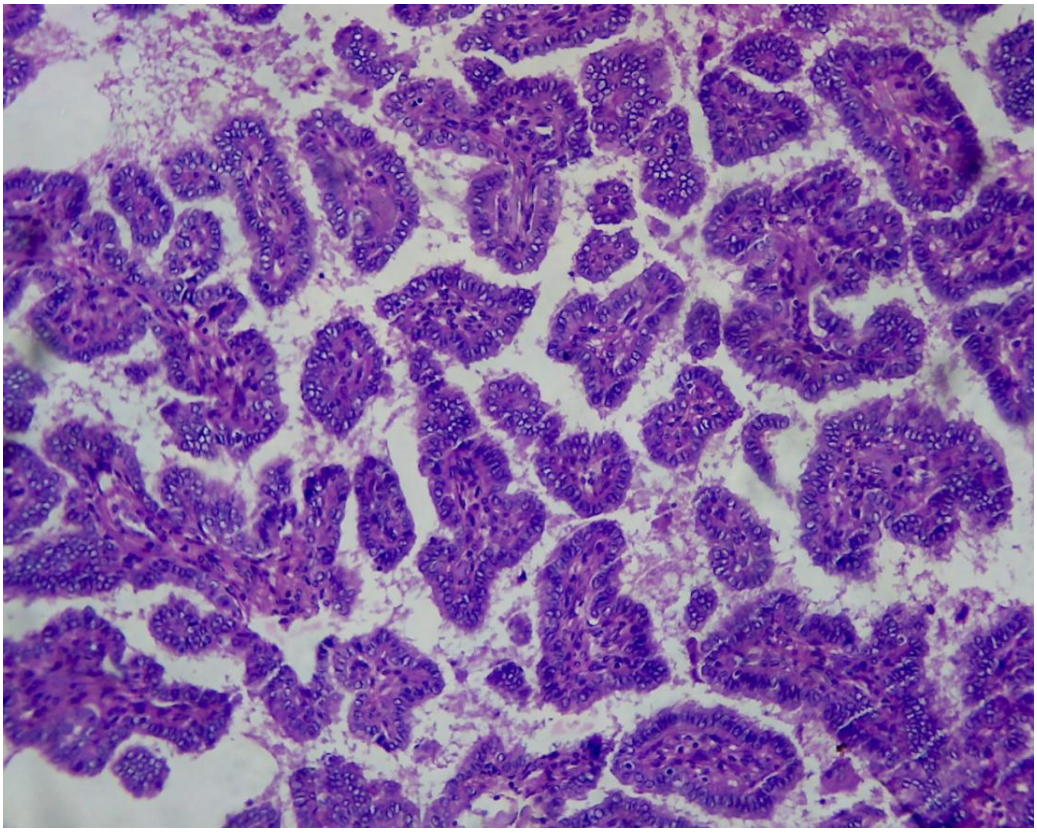


Figure 18 : Numerous papillae in Papillary carcinoma thyroid (10X), H&E stain.

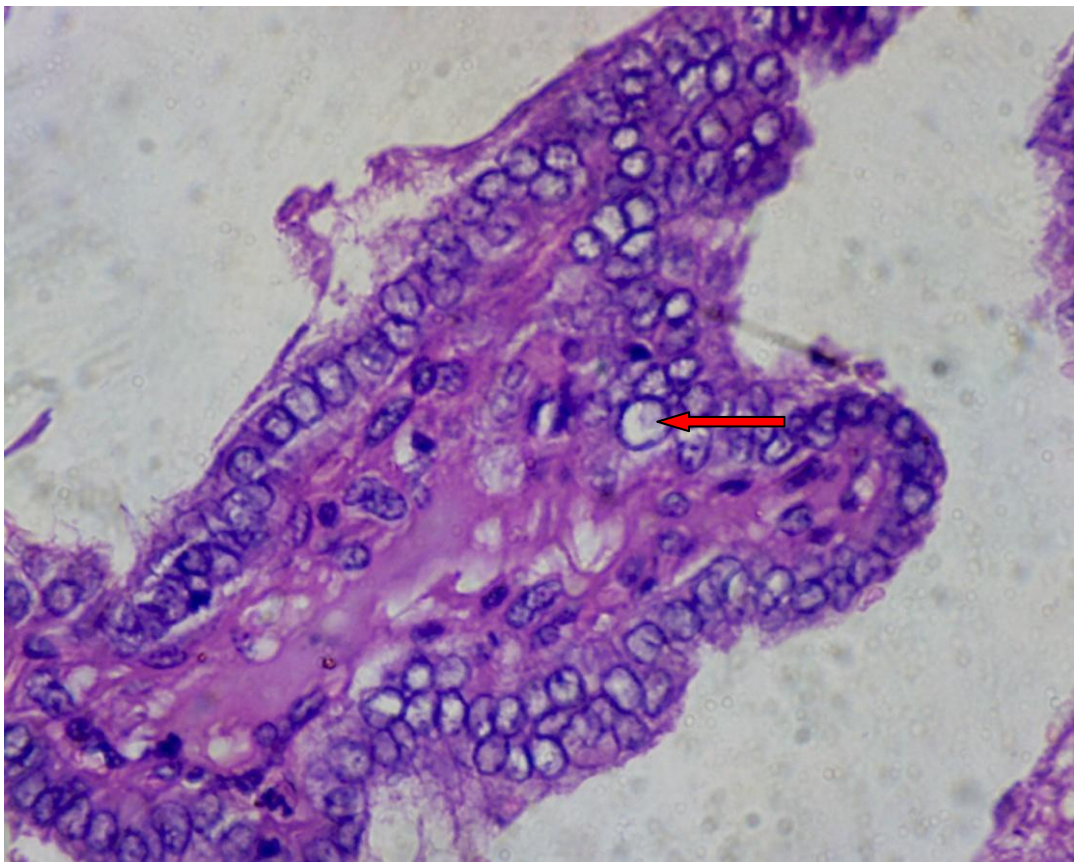


Figure 19: Intranuclear cytoplasmic inclusion in Papillary carcinoma thyroid (40X), H&E stain

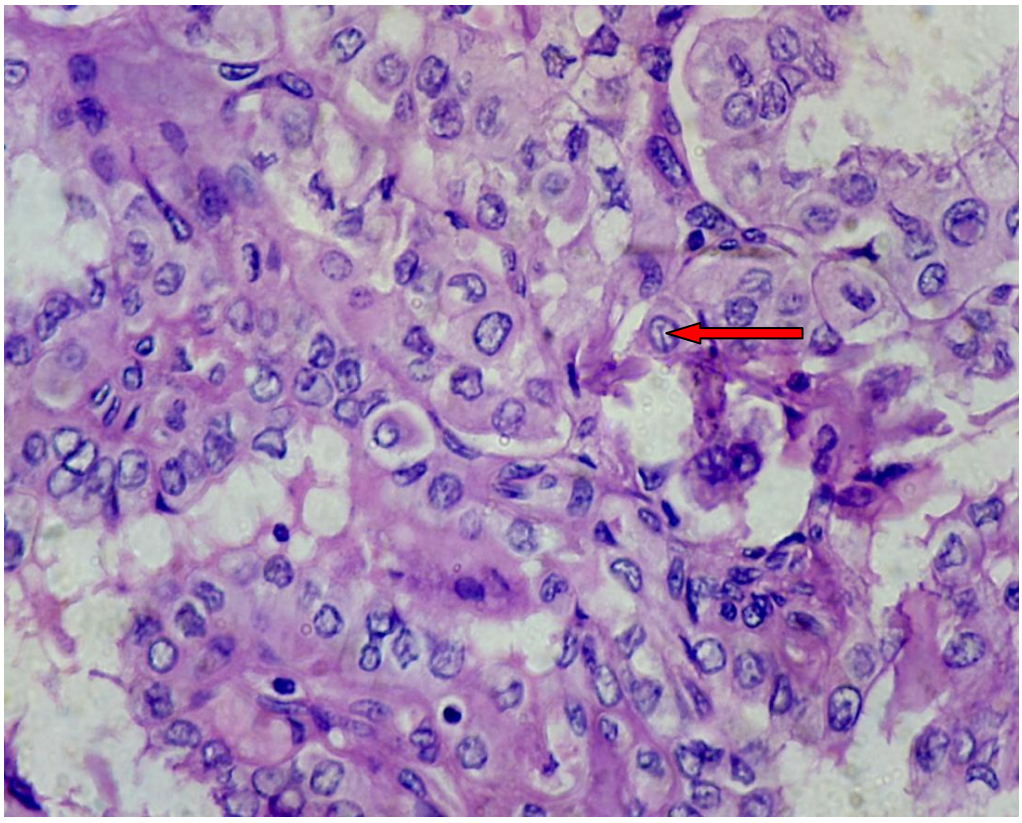


Figure 20 : Nuclear groove in Papillary carcinoma thyroid (40X), H&E stain

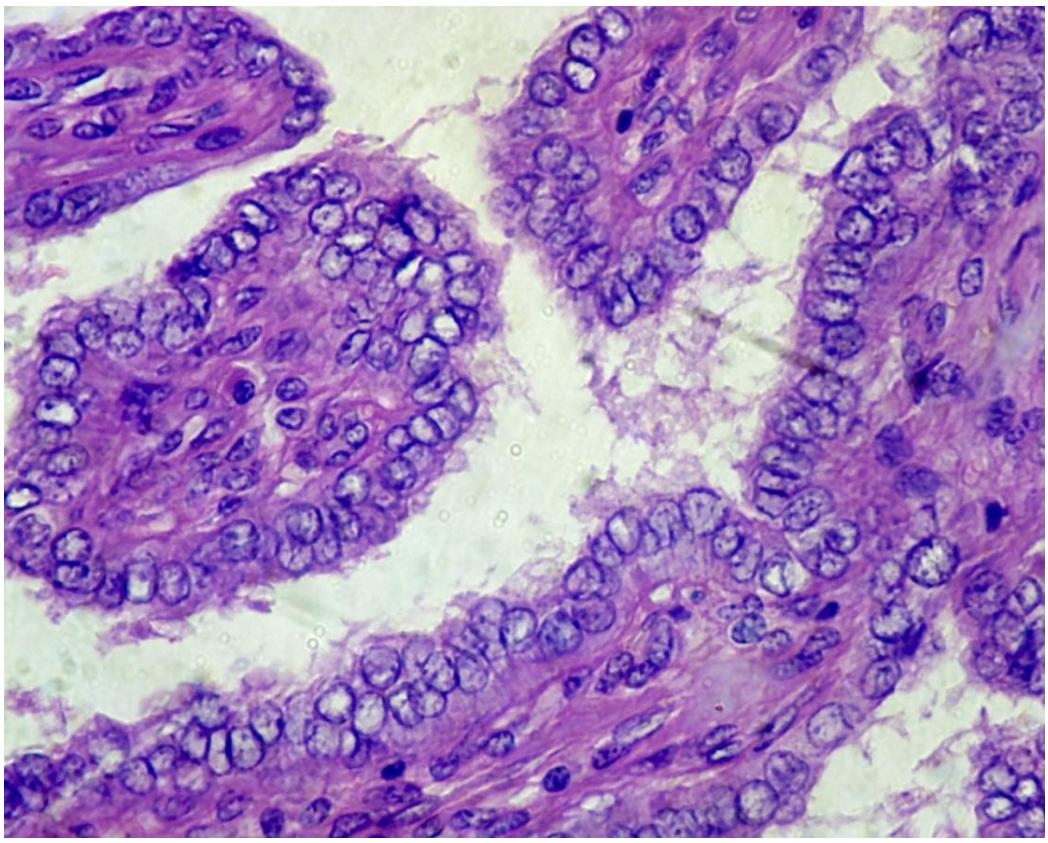


Figure 21: Ground glass nuclei with nuclear crowding and overlapping in Papillary carcinoma thyroid (40X), H&E stain

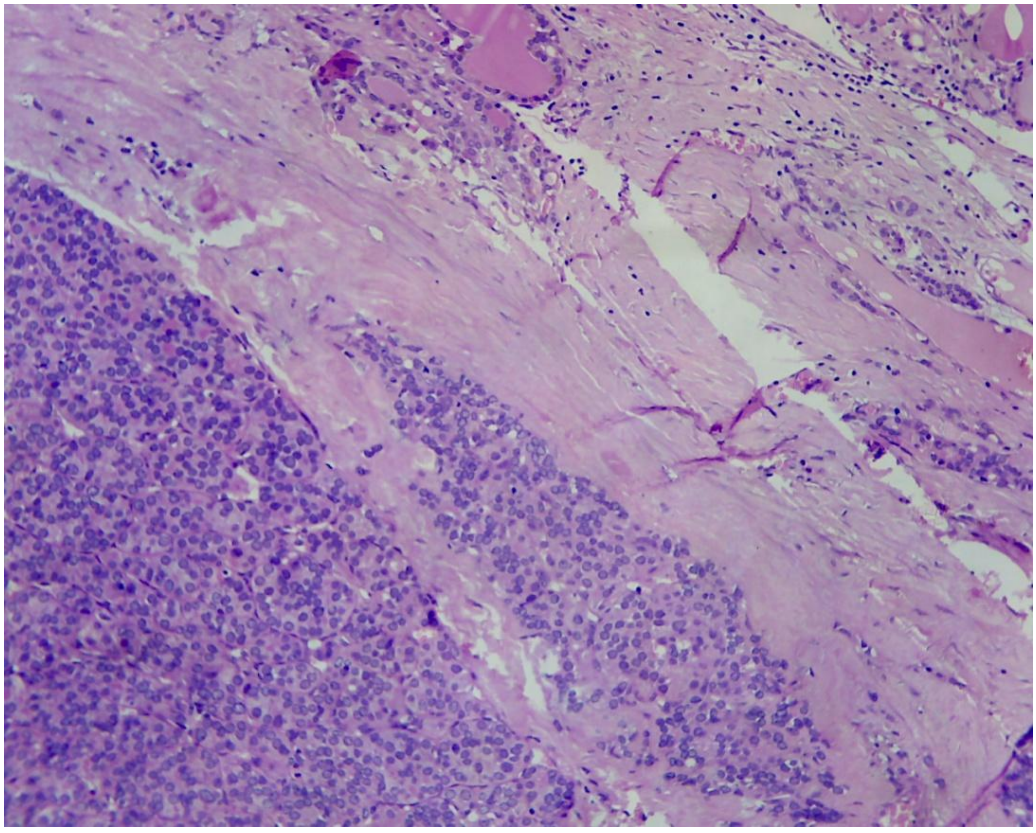


Figure 22 : Capsule invasion in Follicular carcinoma (40X), H&E stain.

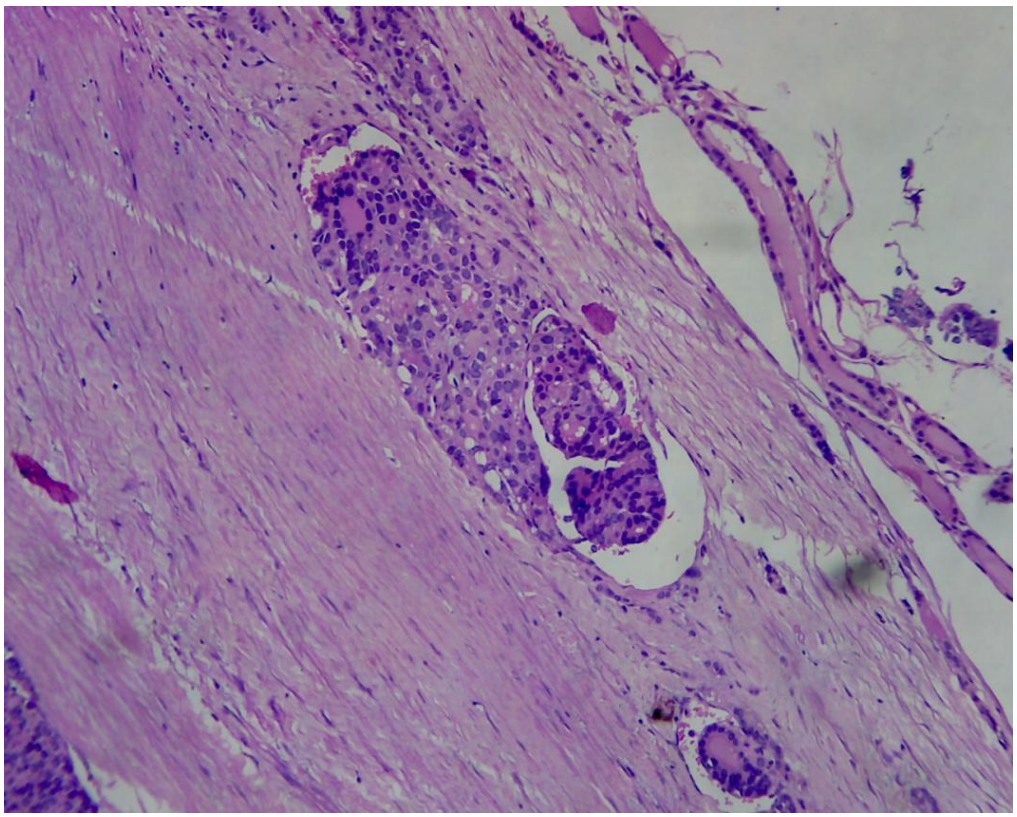


Figure 23 : Vascular invasion in Follicular carcinoma thyroid (40X), H&E stain.

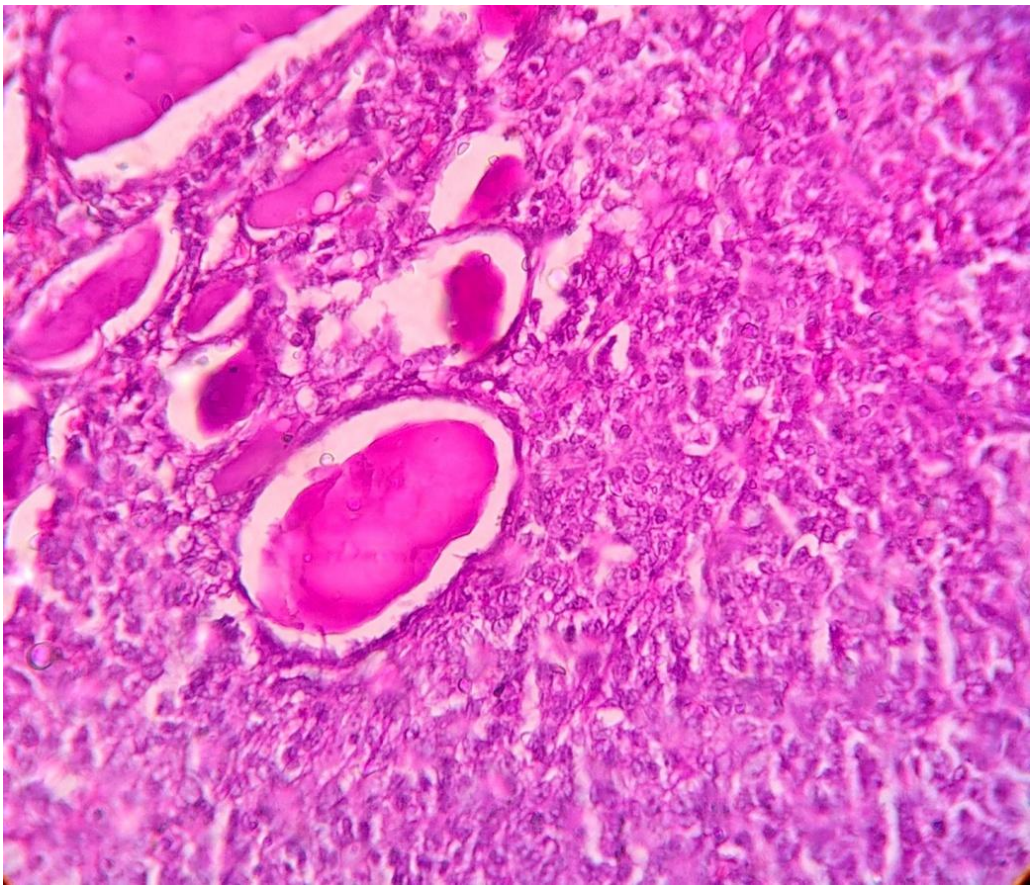


Figure 24 : MALT lymphoma thyroid (40X), H&E stain.

Discussion

DISCUSSION

In this study thyroid fine needle aspirations were categorized according to The Bethesda system, a six tier category. The study period was from July 2015 to June 2016. During the study period, a total of 143 cases of thyroid fine needle aspirations were collected and categorized according to "The Bethesda System for Reporting Thyroid Cytopathology". Later these cases were followed up with their histopathological diagnosis.

Comparison of age incidence of thyroid lesions:

The mean age of presentation of patients in present study was 32.77± 7.284.

Table-14 : Comparison of age incidence of Thyroid lesions

STUDY	AGE RANGE (years)	MEAN AGE (years)
Naz et al[64]	14-84	39.7
Ji Hye Park et al[65]	14-86	50
Gupta et al[66]	22-58	38.7
Present Study	9-80	32.7

The mean age of study of Gupta et al[66] (38.7) and Naz et al[64] (39.7) was comparable to the current study (32.7) The mean age of Ji Hye Park et al[65] (50) study was higher than the present study.

Comparison of Sex incidence of thyroid lesions

The Female to male ratio obtained in the present study is 3:1

Table -15: Comparison of sex incidence of Thyroid lesions

STUDY	FEMALES	MALES	TOTAL No. OF CASES	FEMALE:MALE RATIO
Naz et al[64]	413	115	528	3.6:1
Ji Hye park et al[65]	1217	321	1538	3.8:1
Melo Uribe et al[67]	174	22	196	7.9:1
Present study	108	35	143	3:1

Thyroid lesions are more prevalent in females, this is seen in present study and it was comparable with studies of Naz et al,[64] Ji Hye Park et al,[65] and Melo Cribe et al.[67] In the study of Melo Cribe et al[67] the ratio of female to male ratio was higher.

Adequacy rate of the aspirates:

The adequacy rate of the present study was 96%.

Table -16: Comparison of adequacy rate

STUDY	ADEQUACY RATES (%)
Melo Uribe et al[67]	95.6
Naz et al[64]	94
Handa et al[68]	94.9
Present study	96

The adequacy rate of the current study was comparable with studies of Melo Uribe et al,[67] Naz et al,[64] and Handa et al.[68]

Non neoplastic and neoplastic lesions :

Table -17 : Comparison of non neoplastic and neoplastic lesions

STUDY	NON NEOPLASTIC	NEOPLASTIC	RATIO
Tabaqchali et al[69]	145	94	1.54:1
Handa et al[68]	381	31	12.3:1
Melo uribe et al [67]	75	105	0.75:1
Present study	119	19	6.2:1

Non neoplastic lesions were common in the present study, this was in concordance with study by Handa et al.[68] The studies of Tabaqchali et al,[69] and Melo uribe et al[67] had nearly equal incidence of non neoplastic and neoplastic lesions, this may be probably because of the studies being conducted in oncology institutes.

Comparison of incidence of The Bethesda categories:

TABLE – 18: Comparison of incidence of Bethesda categories

Study	**Bethesda I**	**Bethesda II**	**Bethesda III**	**Bethesda IV**	**Bethesda V**	**Bethesda VI**
Ji Hye Park et al[65]	13.3%	40.6%	9.1%	0.4%	19.3%	17.3%
Vickie Y Jo et al[70]	18.6%	59%	3.4%	9.7%	23%	7%
Mondol et al[71]	1.2%	87.5%	1%	4.2%	1.4%	4.7%
Present study	3.4%	83.21%	0%	9.1%	2.1%	2.1%

The incidence of lesions in all categories of present study was comparable with the study of Mondol et al.[71] Incidence of category I lesions were far lower than the studies of Ji Hye Park et al[65] and Vickie Y Jo et al,[70] owing to the repetition of FNA if they are inconclusive. There were no lesions in category III in the present study.

Comparison of malignancy rates :

Table- 19: Comparison of malignancy rates

Study	**I**	**II**	**III**	**IV**	**V**	**VI**
Vickie Y Jo et al[70]	8.9%	1.1%	17%	25.4%	70%	98.1%
Yassa et al[72]	10%	0.3%	24%	28%	60%	97%
Mondol et al[71]	0%	4.5%	20%	30.6%	75%	97.8%
Yang et al[35]	10.9%	7.3%	13.5%	32.2%	64.7%	98.6%
Present study	0%	3.4%	0%	46%	66%	100%

The incidence of malignancy rates according to the Bethesda system for category II is 0-3%, category III is 5-15%, category IV is 15 -30%, category V is 60-75%, category VI is 97-99%. The percentage of occurrence of malignancies in each category of the present study was in concordance with all categories except category IV. In category IV, present study had higher incidence of malignancy, probably of missing Follicular variant of Papillary carcinoma which was thought to be as Follicular neoplasm.

Comparison of statistical indices

Table- 20: Comparison of statistical indices

Study	Sensitivity	Specificity	PPV	NPV
Gupta M et al[66]	80%	86.6%	80%	86.6%
Handa et al[68]	97%	100%	96%	100%
Tabaqchali et al[69]	86.8%	67%	65.5%	87.5%
Present study	20%	100%	100%	91.1%

In the present study specificity, positive predictive value and negative predictive value were all in concordance with studies of Gupta et al,[66] Handa et al[68] and Tabaqchali et al.[69] Even the specificity and positive predictive value were 100% which implies the efficacy of the FNA performed in our institution.

The low rate of sensitivity may be due to small sample size, smaller size of malignant lesion in a large gland.

Summary & Conclusion

SUMMARY

"The Bethesda system for reporting thyroid cytopathology and its histopathological correlation" was a cross sectional study conducted in the Department of Pathology, Coimbatore Medical College, Coimbatore, for a period of 1 year from July 2015 to June 2016. The Present study was undertaken to categorize thyroid fine needle aspirations according to "The Bethesda system" taking histopathology as the gold standard.

The salient features of the present study include :

- A total of 143 cases were studied, out of which 108 patients were females and 35 were males.
- Age group of these patients ranged from 9 years to 80 years with a mean age of 32.7 years. Majority of the patients were in the age group of 31- 40 years.
- An adequacy rate of 96 % was obtained in the study.
- Out of 143 cases, 119 cases were non – neoplastic, 19 cases were neoplastic, and 5 cases were unsatisfactory for evaluation.
- The benign category (category II) had the maximum number of cases(119 cases), out of which colloid goiter was the predominant diagnosis(70 cases).

- There were no cases in the category III.

- Category IV had 13 cases, out of which 7 cases turned out to be benign in histopathology, among the remaining 6 cases , 4 cases were Papillary carcinoma, 1 case each of Follicular Carcinoma and Lymphoma.

- Category V had 3 cases, among them one case was Multinodular goiter, one was Follicular carcinoma and the remaining one was Follicular variant of Papillary carcinoma.

- Category VI had 3 cases of Papillary carcinoma and there was 100 % histopathological correlation in the malignancy category.

- The malignancy rate in the present study ranged from 3.4% in category II to 100 % in category VI.

- The sensitivity and specificity of The Bethesda system was 20% and 100 % respectively. The positive predictive value was 100% and the negative predictive value was 91.1%.

- The sensitivity rates were far less than similar studies which may give a false impression to the surgeon, but this may be due to limited sample size.

CONCLUSION

Thyroid swellings are still an enigma to the surgeon and the pathologist. Diagnostic accuracy of cytopathology is proven by the present study with 100% specificity and 100% PPV. Thus, as a screening test before surgery, FNAC still needs to be followed as a routine procedure for successful patient management.

Adequacy rate of the present study is 96%. This can be further enhanced by further imaging technique like ultrasound.

Category I and II in the non neoplastic category of The Betheseda system have more accurate categorization index. Similarly category V and VI had precision in the diagnosis. This indicates that there are clearcut distinctions between the two ends of the spectrum of non neoplastic and neoplastic lesions.

However category III had no cases and category IV had high discordant rate. This suggest that there is need of further clarity for diagnostic categorization in this grey zone. It could be further refined by applying more advanced immunocytochemical and molecular genetic analysis to these patients falling in the grey zone.

Further studies involving larger sample size and with specialized techniques is the need of the hour for patients with thyroid swelling.

References

REFERENCES

1. Sadler TW. Langman's medical embryology. Lippincott Williams & Wilkins; 2011 Dec 15.

2. Doniach I. The thyroid gland. In:Symmers WStC (ed.) *Systemic Pathology,*vol 4, 2nd edn. Edinburgh: ChurchillLivingstone; 1978:1975-2037.

3. Tangpricha V, Chen BJ, Swan NC, Sweeney AT, De las Morenas A, Safer JD. Twenty-one-gauge needles provide more cellular samples than twenty-five-gauge needles in fine-needle aspiration biopsy of the thyroid but may not provide increased diagnostic accuracy. Thyroid. 2001 Oct 1;11(10):973-6.

4. Werga P, Wallin G, Skoog L, Hamberger B. Expanding role of fine-needle aspiration cytology in thyroid diagnosis and management. World journal of surgery. 2000 Aug 1;24(8):907-12.

5. Hamburger JI, Husain MU, Nishiyama R, Nunez C, Solomon D. Increasing the accuracy of fine-needle biopsy for thyroid nodules. Archives of pathology & laboratory medicine. 1989 Sep;113(9):1035-41.

6. Soderstrom N. Identification of normal tissue and tumors by cytologic aspiration biopsy. *Acta Soc Med* 1958;65:53-87.

7. Guidelines of The Papanicolaou Society of Cytopathology for the examination of fine-needle aspiration specimens from thyroid nodules: The Papanicolaou Society of Cytopathology Task Force on Standards of Practice Diagn Cytopathol 1996;15:84-9

8. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Sherman SI, Tuttle RM. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Taskforce. Thyroid. 2006 Feb 1;16(2):109-42.

9. AACE/AME Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocrine Practice. 2006 Oct 26.

10. Ali SZ, Cibas E, editors. The Bethesda system for reporting thyroid cytopathology: definitions, criteria and explanatory notes. Springer Science & Business Media; 2010 Mar 20.

11. Kapur U, Wojcik EM. Follicular neoplasm of the thyroid—vanishing cytologic diagnosis?. Diagnostic cytopathology. 2007 Aug 1;35(8):525-8.

12. Nguyen GK, Ginsberg J, Crockford PM. Fine-needle aspiration biopsy cytology of the thyroid. Its value and limitations in the diagnosis and management of solitary thyroid nodules. Pathol Annu. 1991;26 :63-91.

13. Jing X, Michael CW, Pu RT. The clinical and diagnostic impact of using standard criteria of adequacy assessment and diagnostic terminology on thyroid nodule fine needle aspiration. Diagnostic cytopathology. 2008 Mar 1;36(3):161-6.

14. Goellner JR, Gharib H, Grant CS, Johnson DA. Fine needle aspiration cytology of the thyroid, 1980 to 1986. Acta cytologica. 1986 Dec;31(5):587-90.

15. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association (ATA) guidelines taskforce on thyroid nodules and differentiated thyroid cancer. Thyroid. 2009 Nov 1;19(11):1167-214.

16. Gharib HO, Goellner JR, Johnson DA. Fine-needle aspiration cytology of the thyroid. A 12-year experience with 11,000 biopsies. Clinics in laboratory medicine. 1993 Sep;13(3):699-709.

17. Malle D, Valeri R, Pazaitou-Panajiotou K, Kiziridou A, Vainas I, Destouni C. Use of a thin-layer technique in thyroid fine needle aspiration. Acta cytologica. 2006 Jul 1;50(1):23-7.

18. Clark DP, Faquin WC. Thyroid cytopathology. Springer Science & Business Media; 2010 Jun 17..

19. Orell SR. The thyroid: fine-needle biopsy and cytological diagnosis of thyroid lesions. Karger Medical and Scientific Publishers; 1997.

20. Hurthle K. A study of the secretory process of the thyroid gland. Arch F D Ges Physio. 1894:56.

21. Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, Vielh P, DeMay RM, Sidawy MK, Frable WJ. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. Diagnostic cytopathology. 2008 Jun 1;36(6):425-37.

22. Söderström N, Nilsson G. Cytologic diagnosis of thyrotoxicosis Acta Med Scand. 1979;205(4):263-5

23. Jayaram GI, Marwaha RK, Gupta RK, Sharma SK. Cytomorphologic spects of thyroiditis. A study of 51 cases with functional, immunologic and ultrasonographic data. Acta cytologica. 1986 Dec;31(6):687-93.

24. Pitman MB, Abele J, Ali SZ, Duick D, Elsheikh TM, Jeffrey RB, Powers CN, Randolph G, Renshaw A, Scoutt L. Techniques for thyroid FNA: A synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. Diagnostic cytopathology. 2008 Jun 1;36(6):407-24.

25. Lu CP, Chang TC, Wang CY, Hsiao YL. Serial changes in ultrasound-guided fine needle aspiration cytology in subacute thyroiditis. Acta cytologica. 1997 Jul 1;41(2):238-43.

26. Priyanthi Kumarasinghe M, De Silva S. Pitfalls in cytological diagnosis of autoimmune thyroiditis. Pathology. 1999 Jan 1;31(1):1-7.

27. MacDonald L, Yazdi HM. Fine needle aspiration biopsy of Hashimoto's thyroiditis. Acta cytologica. 1999 Jul 1;43(3):400-6.

28. Tulecke MA, Wang HH. ThinPrep® for cytologic evaluation of follicular thyroid lesions: Correlation with histologic findings. Diagnostic cytopathology. 2004 Jan 1;30(1):7-13.

29. Cochand-Priollet B, Prat JJ, Polivka M, Thienpont L, Dahan H, Wassef M, Guillausseau PJ. Thyroid fine needle aspiration: the morphological features on ThinPrep® slide preparations. Eighty cases with histological control. Cytopathology. 2003 Dec 1;14(6):343-9.

30. Frost AR, Sidawy MK, Ferfelli M, Tabbara SO, Bronner NA, Brosky KR, Sherman ME. Utility of thin-layer preparations in thyroid fine-needle aspiration. Cancer Cytopathology. 1998 Feb 25;84(1):17-25.

31. Layfield LJ, Abrams J, Cochand-Priollet B, Evans D, Gharib H, Greenspan F, Henry M, LiVolsi V, Merino M, Michael CW, Wang H. Post-thyroid FNA testing and treatment options: A synopsis of the National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. Diagnostic cytopathology. 2008 Jun 1;36(6):442-8.

32. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Annals of internal medicine. 1993 Feb 15;118(4):282-9.

33. Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, Moore FD, Kim BW, Nosé V, Marqusee E, Larsen PR. Long-term assessment

of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer Cytopathology. 2007 Dec 25;111(6):508-16.

34. Nayar R, Ivanovic M. The indeterminate thyroid fine-needle aspiration. Cancer Cytopathology. 2009 Jun 25;117(3):195-202.

35. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: A study of 4703 patients with histologic and clinical correlations. Cancer Cytopathology. 2007 Oct 25;111(5):306-15.

36. Baloch ZW, Fleisher S, LiVolsi VA, Gupta PK. Diagnosis of "follicular neoplasm": A gray zone in thyroid fine-needle aspiration cytology. Diagnostic cytopathology. 2002 Jan 1;26(1):41-4.

37. Schlinkert RT, Van Heerden JA, Goellner JR, Gharib H, Smith SL, Rosales RF, Weaver AL. Factors that predict malignant thyroid lesions when fine-needle aspiration is "suspicious for follicular neoplasm". InMayo Clinic Proceedings 1997 Oct 31 (Vol. 72, No. 10, pp. 913-916). Elsevier.

38. Kelman AS, Rathan A, Leibowitz J, Burstein DE, Haber RS. Thyroid cytology and the risk of malignancy in thyroid nodules: importance of nuclear atypia in indeterminate specimens. Thyroid. 2001 Mar 1;11(3):271-7.

39. Renshaw AA, Wang E, Wilbur D, Hughes JH, Haja J, Henry MR. Interobserver agreement on microfollicles in thyroid fine-needle aspirates. Archives of pathology & laboratory medicine. 2006 Feb;130(2):148-52.

40. Elsheikh TM, Asa SL, Chan JK, DeLellis RA, Heffess CS, LiVolsi VA, Wenig BM. Interobserver and intraobserver variation among experts in the diagnosis of thyroid follicular lesions with borderline nuclear features of papillary carcinoma. American journal of clinical pathology. 2008 Nov 1;130(5):736-44.

41. DeLellis RA, editor. Pathology and genetics of tumours of endocrine organs. IARC; 2004.

42. French CA, Alexander EK, Cibas ES, Nose V, Laguette J, Faquin W, Garber J, Moore F, Fletcher JA, Larsen PR, Kroll TG. Genetic and biological subgroups of low-stage follicular thyroid cancer. The American journal of pathology. 2003 Apr 30;162(4):1053-60.

43. Nikiforova MN, Biddinger PW, Caudill CM, Kroll TG, Nikiforov YE. PAX8-PPARγ rearrangement in thyroid tumors: RT-PCR and immunohistochemical analyses. The American journal of surgical pathology. 2002 Aug 1;26(8):1016-23.

44. Renshaw AA. Accuracy of thyroid fine-needle aspiration using receiver operator characteristic curves. American journal of clinical pathology. 2001 Oct 1;116(4):477-82.

45. Wang HH. Reporting thyroid fine-needle aspiration: Literature review and a proposal. Diagnostic cytopathology. 2006 Jan 1;34(1):67-76.

46. Baloch ZW, LiVolsi VA. Fine-needle aspiration of thyroid nodules: past, present, and future. Endocrine Practice. 2004 Aug 13.

47. Renshaw AA. "Histiocytoid" cells in fine-needle aspirations of papillary carcinoma of the thyroid. Cancer Cytopathology. 2002 Aug 25;96(4):240-3.

48. Rupp M, Ehya H. Nuclear grooves in the aspiration cytology of papillary carcinoma of the thyroid. Acta cytologica. 1988 Dec;33(1):21-6.

49. Ellison E, Lapuerta P, Martin SE. Psammoma bodies in fine-needle aspirates of the thyroid. Cancer Cytopathology. 1998 Jun 25;84(3):169-75.

50. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Sherman SI, Tuttle RM. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Taskforce. Thyroid. 2006 Feb 1;16(2):109-42.

51. Papotti M, Manazza AD, Chiarle R, Bussolati G. Confocal microscope analysis and tridimensional reconstruction of papillary thyroid carcinoma nuclei. Virchows Archiv. 2004 Apr 1;444(4):350-5.

52. Agrawal S, Rao RS, Parikh DM, Parikh HK, Borges AM, Sampat MB. Histologic trends in thyroid cancer 1969–1993: A clinico-pathologic analysis of the relative proportion of anaplastic carcinoma of the thyroid. Journal of surgical oncology. 1996 Dec 1;63(4):251-5.

53. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the US, 1985-1995. Cancer. 1998 Dec 15;83(12):2638-48.

54. Lam KY, Lo CY, Chan KW, Wan KY. Insular and anaplastic carcinoma of the thyroid: a 45-year comparative study at a single institution and a review of the significance of p53 and p21. Annals of surgery. 2000 Mar 1;231(3):329-38.

55. Aldinger KA, Samaan NA, Ibanez M, Hill CS. Anaplastic carcinoma of the thyroid. A review of 84 cases of spindle and giant cell carcinoma of the thyroid. Cancer. 1978 Jun 1;41(6):2267-75.

56. Lang BH, Lo CY. Surgical options in undifferentiated thyroid carcinoma. World journal of surgery. 2007 May 1;31(5):969-77.

57. Venkatesh YS, Ordonez NG, Schultz PN, Hickey RC, Goepfert H, Samaan NA. Anaplastic carcinoma of the thyroid. Cancer. 1990 Jul 15;66:321-30.

58. Disibio G, French SW. Metastatic patterns of cancers: results from a large autopsy study. Archives of pathology & laboratory medicine. 2008 Jun;132(6):931-9.

59. Czech JM, Lichtor TR, Carney JA, Van Heerden JA. Neoplasms metastatic to the thyroid gland. Surgery, gynecology & obstetrics. 1982 Oct;155(4):503-5.

60. IVY HK. Cancer metastatic to the thyroid: a diagnostic problem. InMayo Clinic Proceedings 1984 Dec 31 (Vol. 59, No. 11, pp. 856-859). Elsevier.

61. Shimaoka K, Sokal JE, Pickren JW. Metastatic neoplasms in the thyroid gland. Pathological and clinical findings. Cancer. 1962 May 1;15(3):557-65.

62. Schröder S, Bürk CG, de Heer K. [Metastases of the thyroid gland--morphology and clinical aspects of 25 secondary thyroid neoplasms]. Langenbecks Archiv fur Chirurgie. 1986 Dec;370(1):25-35.

63. Derringer GA, Thompson LD, Frommelt RA, Bijwaard KE, Heffess CS, Abbondanzo SL. Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases. The American journal of surgical pathology. 2000 May 1;24(5):623-39.

64. Naz S, Hashmi AA, Faridi N, Edhi MM, Kamal A, Khan M. Diagnostic accuracy of Bethesda system for reporting thyroid cytopathology: an institutional perspective. International archives of medicine. 2014 Oct 31;7(1):1.

65. Ji Hye Park, Sun Och Yoon, Eun Ju Son, Hye Min Kim, Ji Hae Nahm, SoonWon Hong. Incidence and Malignancy Rates of Diagnoses in the Bethesda System for Reporting Thyroid Aspiration Cytology: An Institutional Experience. Korean J Pathol. 2014 Apr; 48(2): 133–139.

66. Manoj Gupta, Savita Gupta, and Ved Bhushan Gupta, "Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule," Journal of Thyroid Research, vol. 2010, Article ID 379051, 5 pages, 2010. doi:10.4061/2010/379051

67. Melo-Uribe Mario Alexander, Sanabria Álvaro, Romero-Rojas Alfredo, Pérez Gabriel, Vargas Elga Johanna, Abaúnza María Claudia, Gutiérrez Víctor. The Bethesda system for reporting thyroid cytopathology in Colombia: Correlation

with histopathological diagnoses in oncology and non-oncology institutions. J Cytol 2015;32:12-6

68. Handa U, Garg S, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study on 434 patients. Journal of cytology. 2008 Jan 1;25(1):13.

69. Tabaqchali MA, Hanson JM, Johnson SJ, Wadehra V, Lennard TW, Proud G. Thyroid aspiration cytology in Newcastle: a six year cytology/histology correlation study. Annals of the Royal College of Surgeons of England. 2000 May;82(3):149.

70. Jo VY, Stelow EB, Dustin SM, Hanley KZ. Malignancy risk for fine-needle aspiration of thyroid lesions according to the Bethesda System for Reporting Thyroid Cytopathology. American journal of clinical pathology. 2010 Sep 1;134(3):450-6.

71. Mondal SK, Sinha S, Basak B, Roy DN, Sinha SK. The Bethesda system for reporting thyroid fine needle aspirates: A cytologic study with histologic follow-up. Journal of Cytology. 2013 Apr 1;30(2):94.

72. Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, Moore FD, Kim BW, Nosé V, Marqusee E, Larsen PR. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer Cytopathology. 2007 Dec 25;111(6):508-16.

Annexures

ANNEXURE I: PROFORMA

NAME :

AGE :

SEX :

DATE :

OP/IP NO :

PRESENTING COMPLAINTS:

PAST HISTORY :

PRE DIAGNOSIS :

FNAC NO :

FNAC DIAGNOSIS :

BIOPSY NO :

HISTOPATHOLOGICAL DIAGNOSIS:

CONSENT FORM

Dr. LEELAVATHY G post graduate student in the Department of Pathology, Coimbatore Medical College is conducting a study on "**The Bethesda System of Reporting Thyroid Cytopathology and its histopathological correlation".** Fine needle aspirations are done for various lesions of thyroid and are processed and examined under a microscope to obtain diagnostic information or is tested for other studies. I have been informed, to my satisfaction regarding the nature of procedure. The data used herein may be used for research and publication.

Name :

Place :

Signature :

ஒப்புதல் படிவம்

பெயர் .

வயது .

பாலினம் .

முகவரி .

அரசு கோவை மருத்துவக் கல்லூரியில் நோய் குறியியல் மருத்தவ துறையில் பட்ட மேற்படிப்பு பயிலும் மாணவி **மரு. க. லீலாவதி** அவர்கள் மேற்கொள்ளும் **"முன் கழுத்துக் கழலைகட்டியில் இருந்து ஊசி மூலம் திசு / நீர் எடுத்து கண்டறிதல்"** பற்றிய ஆய்வு மற்றும் அனைத்து விளக்கங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னை பற்றிய அனைத்து விவரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் இந்த ஆய்வில் இருந்து நான் விலகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம்

தேதி நோயாளியின் கையொப்பம் / ரேகை

ANNEXURE II – STAINING PROTOCOL

PAPANICOLAOU STAINING

REAGENTS REQUIRED:

1. Harri's Haematoxylin
   (Without acetic acid)
2. Orange G 6 (OG 6).
   0.5 Orange G in 95% alcohol 100 ml
   Phosphotungstic acid 0.15g.
3. Eosin azure 36 (EA 36 OR EA 50)
   0.5 Light green SF yellow in 95% alcohol 45ml
   0.5% Bismark brown in 95% alcohol 10 ml
   0.5% Eosin Y in 95% alcohol 45 ml
   Phosphotungstic acid 0.2 g
   Saturated aqueous lithium carbonate 1 drop

TECHNIQUE :

1. Fix smears (while still moist) in 95% alcohol – 15 minutes.
2. Rinse smears in distilled water.
3. Stain in Harri's haematoxylin for 4 minutes.
4. Wash in tap water for 1-2 minutes.
5. Differentiate in acid alcohol (25% HCL in 70% alcohol).
6. Blue in tap water or 1.5% sodium bicarbonate.
7. Rinse in distilled water.

8. Transfer to 70% alcohol, then 95% alcohol for a few seconds.

9. Stain in OG 6 for 1-2 minutes.

10. Rinse in 3 changes of 95% alcohol for a few seconds.

11. Stain in EA 50 for 3 – 5 minutes.

12. Rinse in 3 changes of 95% alcohol for a few seconds.

MAY GRUNWALD GIEMSA STAINING :

Stock Solution of MGG:

0.5 grams of MGG powder dissolved in 100 ml of methanol.

Stock Solution of Giemsa:

0.75 grams of Giemsa Powder dissolved in 100 ml of methanol.

Working Solution of MGG:

Two parts of Stock Solution Of MGG and one part of methanol.

Working Solution of Giemsa:

One part of Stock Solution of Giemsa and nine parts of distilled water.

Staining Technique:

Stain with Working Solution of MGG for 1-2 minutes.

Dilution with Working Solution of Giemsa 10 minutes and wash in tap water and dry.

HEMATOXYLIN AND EOSIN STAINING:

1. Hematoxylin and Eosin stain
2. Deparaffinize sections in xylene by immersing for 30 seconds.
3. Place the sections in isopropyl alcohol for 15 minutes
4. Wash in running tap water
5. Stain in Erhlich's hematoxylin for 10 to 15 minutes
6. Differentiation is done with 1% acid alcohol two to three dips
7. Blueing is carried out for 10 minutes
8. Counterstain with Eosin 1% solution 3 to 4 dips
9. Wash in running tap water
10. Air dry

ANNEXURE - III

LIST OF ABBREVIATIONS

AFLUS	–	Atypical Follicular Lesion of Undetermined Significance
AUS	–	Atypia of Undetermined Significance
ATA	–	American Thyroid Association
BFN	–	Benign Follicular Nodule
CEA	–	Carcino Embryonic Antigen
DLBCL	–	Diffuse Large B cell Lymphoma
DPX	–	Dextrene Polystrene Xylene
FLUS	–	Follicular Lesion of Undetermined Significance
FN	–	False Negative
FN/SFN	–	Follicular Neoplasm/Suspicious of Follicular Neoplasm
FNA	–	Fine Needle Aspiration
FNAC	–	Fine Needle Aspiration Cytology
FNHCT/ SFNHCT	–	Follicular neoplasm,Hürthle cell type/ Suspicious for a Follicular neoplasm, Hürthle cell type
FP	–	False Positive

GD – Grave's Disease

INCI – Intranuclear Cytoplasmic Inclusion

LT – Lymphocytic Thyroiditis

MALT – Mucosa Associated Lymphoid Tissue

MGG – May Grundwald Giemsa

MNG – Multinodular Goiter

MTC – Medullary Thyroid Carcinoma

N/C – Nuclear - Cytoplasmic

NCI – National Cancer Institute

ND/UNS – Non –diagnostic/ Unsatisfactory

NG – Nodular goitre

NHL – Non Hodgkin's Lymphoma

NPV – Negative Predictive Value

PAX-8–*PPAR* γ – Paired Box- Peroxisome Proliferator Activated Receptor

PB – Psammoma Body

PDTC – Poorly Differentiated thyroid Carcinoma

PPV – Positive Predictive Value

PTC – Papillary Thyroid Carcinoma

RET – Rearranged During Transfection

SD – Standard Deviation

SFM – Suspicious For Malignancy

SIAPEC – Italian Society of Anatomic Pathology and Cytopathology

SPSS – Statistical Package for Social Sciences

SQC – Squamous Cell Carcinoma

TBSRTC – The Bethesda System Of Reporting Thyroid Cytopathology

TN – True Negative

TP – True Positive

TTF 1 – Thyroid Transcription Factor

UTC – Undifferentiated Thyroid Carcinoma

US – Ultrasound

WHO – World Health Organisation

ANNEXURE - IV

MASTER CHART

S.NO	AGE	SEX	FNAC NO	CONVENTIONAL FNAC DIAGNOSIS	BETHESDA CATEGORY	HPE NO	HPE DIAGNOSIS
1	33	F	2439/14	Nodular Colloid Goitre	II	133/15	Hashimoto's thyroiditis
2	33	F	2059/14	Nodular Colloid Goitre	II	260/15	Papillary microcarcinoma
3	31	F	2100/14	Hashimoto's thyroiditis	II	360/15	Hashimoto's thyroiditis
4	30	F	33/15	Follicular neoplasm	IV	373/15	Adenomatous goitre
5	35	F	256/15	Cystic degeneration in NCG	II	410/15	Nodular goitre
6	31	F	140/15	Cystic degeneration in NCG	II	411/15	Nodular goitre
7	50	F	109/15	Cystic degeneration in NCG	II	480/15	Nodular goitre
8	45	M	253/15	Cystic degeneration in NCG	II	507/15	Nodular goitre
9	37	F	2870/14	Cystic degeneration in NCG	II	619/15	Adenomatous goitre
10	30	F	139/15	Cystic degeneration in NCG	II	647/15	Hashimoto's thyroiditis
11	54	F	323/15	Nodular Colloid Goitre	II	667/15	Hashimoto's thyroiditis
12	45	M	361/15	Nodular Colloid Goitre	II	704/15	Hashimoto's thyroiditis
13	40	F	28/15	Nodular Colloid Goitre with suspicious for Papillary carcinoma	V	725/15	Multi nodular goitre
14	50	F	210/15	Cystic degeneration in NCG	II	727/15	Nodular goitre
15	37	F	411/15	Cystic degeneration in NCG	II	811/15	Multi nodular goitre
16	38	F	478/15	Nodular colloid goitre	II	829/15	Multi nodular goitre
17	27	F	547/15	Dominant nodule of nodular goitre / follicular neoplasm	IV	905/15	Papillary carcinoma
18	75	M	2779/14	Papillary carcinoma	VI	1113/15	Papillary carcinoma
19	50	F	509/15	Nodular Colloid Goitre	II	1137/15	Follicular adenoma
20	35	F	686/15	Cystic degeneration in NCG	II	1208/15	Follicular adenoma
21	37	F	567/15	Hashimoto's thyroiditis	II	1255/15	Hashimoto's thyroiditis
22	50	M	543/15	Nodular Colloid Goitre	II	1271/15	Nodular goitre
23	29	F	764/15	Cystic degeneration in NCG	II	1358/15	Hashimoto's thyroiditis
24	57	M	563/15	Cystic degeneration in NCG	II	1458/15	Adenomatous goitre
25	18	F	584/14	Cystic degeneration in NCG	II	1475/15	Follicular adenoma
26	34	F	2599/14	Nodular Colloid Goitre	II	1496/15	Nodular goitre
27	44	F	957/15	Nodular Colloid Goitre	II	1680/15	Follicular adenoma
28	31	F	997/15	Nodular Colloid Goitre	II	1716/15	Nodular goitre
29	65	F	1112/15	Nodular Colloid Goitre	II	1875/15	Multi nodular goitre
30	30	F	2294/14	Nodular Colloid Goitre	II	1925/15	Papillary carcinoma
31	30	F	1176/15	Cystic degeneration in NCG	II	1969/15	Adenomatous goitre
32	44	F	1237/15	Nodular Colloid Goitre	II	2098/15	Nodular goitre

33	27	F	1199/15	Nodular Colloid Goitre	II	2102/15	colloid goiter
34	32	F	1000/15	Adenomatous goitre	II	2107/15	Adenomatous goitre
35	41	F	410/15	Cystic degeneration in NCG	II	2191/15	Nodular goitre
36	40	F	1274/15	Cystic degeneration in NCG	II	2227/15	Nodular goitre
37	42	M	1318/15	Cystic degeneration in NCG	II	2266/15	Nodular goitre
38	49	F	1271/15	Nodular Colloid Goitre	II	2268/15	Nodular goitre
39	45	F	1405/15	Nodular Colloid Goitre	II	2427/15	Nodular goitre
40	50	F	1315/15	Nodular Colloid Goitre	II	2480/15	Nodular goitre
41	29	F	1522/15	Follicular neoplasm with papillary hyperplasia	V	2528/15	Follicular variant of papillary carcinoma
42	30	F	1609/15	Nodular Colloid Goitre	II	2603/15	Nodular goitre
43	45	F	1512/15	Nodular Colloid Goitre	II	2723/15	Nodular goitre
44	34	F	1526/15	Nodular Colloid Goitre	II	2748/15	Nodular goitre
45	38	F	1632/15	Follicular neoplasm with hurthle cell changes	IV	2792/15	Hashimoto's thyroiditis
46	48	F	1678/15	Nodular Colloid Goitre	II	2799/15	Nodular goitre
47	18	M	521/15	Cystic degeneration in NCG	II	2861/15	Nodular goitre
48	19	F	2017/15	Nodular Colloid Goitre	II	3212/15	Nodular goitre
49	42	F	2055/15	Nodular Colloid Goitre	II	3230/15	Nodular goitre
50	40	F	573/13	Nodular Colloid Goitre	II	3233/15	Hashimoto's thyroiditis
51	32	M	1216/15	Adenomatous goitre	II	3262/15	Adenomatous goitre
52	61	F	1942/15	Nodular Colloid Goitre	II	3270/15	Nodular goitre
53	23	F	457/15	Follicular neoplasm	IV	3292/15	Papillary carcinoma
54	30	F	1977/15	Nodular Colloid Goitre	II	3326/15	Nodular goitre
55	35	M	1847/15	Cystic degeneration in NCG	II	3342/15	Multi nodular goitre
56	53	F	2267/15	Cystic degeneration in NCG	II	3439/15	Papillary carcinoma
57	39	F	757/14	Cystic degeneration in NCG	II	3502/15	Nodular goitre
58	35	F	2226/15	Hashimoto's thyroiditis	II	3518/15	Hashimoto's thyroiditis
59	47	F	2270/15	Nodular Colloid Goitre	II	3576/15	Nodular goitre
60	62	M	2224/15	Nodular Colloid Goitre	II	3601/15	Multi nodular goitre
61	9	F	2273/15	Cystic degeneration in NCG	II	3616/15	Nodular goitre
62	52	F	1609/14	Cystic degeneration in NCG	II	3695/15	Nodular goitre
63	63	M	2431/15	Cystic degeneration in NCG	II	3716/15	Nodular goitre
64	50	F	1725/15	Nodular Colloid Goitre	II	3918/15	Multi nodular goitre
65	44	M	2494/15	Follicular neoplasm	IV	3925/15	Follicular variant of papillary carcinoma
66	45	M	2498/15	Nodular Colloid Goitre	II	3938/15	Nodular goitre
67	43	F	2356/15	Nodular Colloid Goitre	II	4017/15	Follicular adenoma
68	55	F	2474/15	Nodular Colloid Goitre	II	4088/15	Adenomatous goitre
69	40	F	2304/15	Nodular Colloid Goitre	II	4115/15	Hashimoto's thyroiditis
70	18	M	2745/15	Nodular Colloid Goitre	II	4171/15	Adenomatous goitre

71	40	M	2591/15	Adenomatous goitre	II	24/16	Adenomatous goitre
72	24	F	2526/15	Nodular Colloid Goitre	II	25/16	Follicular adenoma
73	38	F	2535/15	Nodular Colloid Goitre	II	33/16	Follicular adenoma
74	41	F	2551/15	Cystic degeneration in NCG	II	35/16	Papillary carcinoma
75	47	M	2274/15	Nodular Colloid Goitre	II	43/16	Nodular goitre
76	39	F	2157/15	Cystic degeneration in NCG	II	61/16	Multi nodular goitre
77	74	F	2629/15	Cystic degeneration in NCG	II	89/16	Adenomatous goitre
78	39	F	2723/15	Nodular Colloid Goitre	II	152/16	Adenomatous goitre
79	31	F	2731/15	Adenomatous goitre	II	157/16	Adenomatous goitre
80	57	M	2734/15	Follicular adenoma with Atypia	V	166/16	Follicular carcinoma
81	40	F	2728/15	Nodular Colloid Goitre	II	208/16	Multi nodular goitre
82	16	F	2003/15	Papillary carcinoma	VI	210/16	Papillary carcinoma
83	58	M	2749/15	Cystic degeneration in NCG	II	228/16	Adenomatous goitre
84	29	F	2040/15	Nodular Colloid Goitre	II	229/16	Nodular goitre
85	45	M	2653/15	Follicular neoplasm with hurthle cell changes	IV	292/16	Hashimoto's thyroiditis
86	35	F	2785/15	Nodular Colloid Goitre	II	318/16	nodular goitre with cystic degeneration
87	46	M	548/16	Nodular Colloid Goitre	II	324/16	Nodular goitre
88	41	M	133/16	Follicular neoplasm /dominant nodule of NCG	IV	363/16	Nodular goitre
89	37	F	1772/15	Nodular Colloid Goitre	II	444/16	Hashimoto's thyroiditis
90	25	F	163/16	Nodular Colloid Goitre	II	471/16	Multi nodular goitre
91	66	M	83/16	Nodular colloid goitre	II	486/16	Lymphoma
92	70	F	142/16	Follicular neoplasm /dominant nodule of NCG	IV	506/16	Adenomatous goitre
93	50	F	259/16	Cystic degeneration in NCG	II	824/16	Follicular adenoma
94	46	M	1700/15	Nodular Colloid Goitre	II	832/16	Nodular goitre
95	53	F	1950/15	Nodular Colloid Goitre	II	889/16	Nodular goitre
96	65	M	333/16	Papillary carcinoma	VI	890/16	Papillary carcinoma
97	32	F	1998/15	Adenomatous goitre	II	946/16	Follicular adenoma
98	39	F	375/16	Nodular Colloid Goitre	II	1038/16	Nodular goitre
99	32	F	251/16	Nodular Colloid Goitre	II	1040/16	Hashimoto's thyroiditis
100	46	F	518/16	Nodular Colloid Goitre	II	1082/16	Hashimoto's thyroiditis
101	33	M	526/16	Cystic degeneration in NCG	II	1153/16	Follicular adenoma
102	26	F	607/16	Nodular Colloid Goitre	II	1169/16	Multi nodular goitre
103	21	F	663/16	Nodular Colloid Goitre	II	1234/16	Adenomatous goitre
104	35	F	670/16	Nodular Colloid Goitre	II	1249/16	Multi nodular goitre
105	50	F	738/16	Nodular Colloid Goitre	II	1420/16	Multi nodular goitre
106	42	M	725/16	Nodular Colloid Goitre	II	1433/16	Nodular goitre
107	33	F	703/16	Cystic degeneration in NCG	II	1444/16	Follicular adenoma
108	80	F	685/16	Cystic degeneration in NCG	II	1448/16	Nodular goitre

109	30	F	709/16	Nodular Colloid Goitre	II	1555/16	Adenomatous goitre
110	36	F	268/16	Few thyroid follicular cells	I	1561/16	Adenomatous goitre
111	51	F	809/16	Micro & macro follicles in colloid background	I	1580/16	Multi nodular goitre
112	39	F	748/16	Cystic degeneration in NCG	II	1646/16	Nodular goitre
113	55	M	860/16	Few thyroid follicular cells in colloid background	I	1733/16	Nodular goitre
114	38	F	800/16	Hashimoto's thyroiditis	II	1751/16	Multi nodular goitre
115	43	M	874/16	Nodular Colloid Goitre	II	1755/16	Nodular goitre
116	33	F	899/16	Nodular Colloid Goitre	II	1767/16	Nodular goitre
117	26	M	1012/16	Nodular Colloid Goitre	II	1806/16	Adenomatous goitre
118	56	F	723/16	Cystic degeneration in NCG	II	1841/16	Nodular goitre
119	40	F	863/16	Benign thyroid follicles with cyst macrophages	I	1842/16	Cystic degeneration of Nodular goitre
120	29	F	648/16	Cystic degeneration in NCG	II	1843/16	Adenomatous goitre
121	41	F	873/16	Cystic degeneration in NCG	II	1925/16	Nodular goitre
122	20	M	795/16	Follicular neoplasm/Dominant nodule	IV	1928/16	Papillary carcinoma
123	44	M	801/16	Nodular Colloid Goitre	II	1970/16	Nodular goitre
124	33	F	1022/16	Cystic degeneration in NCG	II	2022/16	Multi nodular goitre
125	32	F	1065/16	Cystic degeneration in NCG	II	2053/16	Adenomatous goitre
126	52	F	945/16	Benign thyroid follicles in colloid background	I	2101/16	Adenomatous goitre
127	16	F	1095/16	Nodular colloid goitre	II	2136/16	Nodular goitre
128	32	F	1100/16	Nodular colloid goitre	II	2153/16	Nodular goitre
129	35	F	905/16	Nodular Colloid Goitre	II	2205/16	Hashimoto's thyroiditis
130	37	F	989/16	Follicular neoplasm/Dominant nodule of NCG	IV	2255/16	Adenomatous goitre
131	28	F	1103/16	Nodular Colloid Goitre	II	2259/16	Nodular goitre
132	41	M	955/16	Nodular Colloid Goitre	II	2270/16	Nodular goitre
133	34	F	940/15	Nodular Colloid Goitre	II	2322/16	Nodular goitre
134	38	F	1040/16	Follicular neoplasm/Dominant nodule of NCG	IV	2422/16	Adenomatous goitre
135	65	F	1249/16	Follicular neoplasm	IV	2437/16	Follicular carcinoma
136	24	F	1285/16	Cystic degeneration in NCG	II	2525/16	Cystic degeneration of Nodular goitre
137	45	F	1401/16	Nodular Colloid Goitre	II	2527/16	Cystic degeneration of Nodular goitre
138	48	M	1312/16	Nodular Colloid Goitre	II	2541/16	Nodular goitre
139	40	F	1253/16	Nodular Colloid Goitre	II	2553/16	Multi nodular goitre
140	22	M	1053/16	Cystic degeneration in NCG	II	2606/16	Follicular adenoma
141	30	F	1325/16	Cystic degeneration in NCG	II	2615/16	Nodular goitre
142	43	F	1900/15	Nodular colloid goitre	II	2616/16	Nodulargoitre
143	26	M	583/16	Follicular neoplasm/ dominant nodule of NCG	IV	86/16	Hashimoto's thyroiditis